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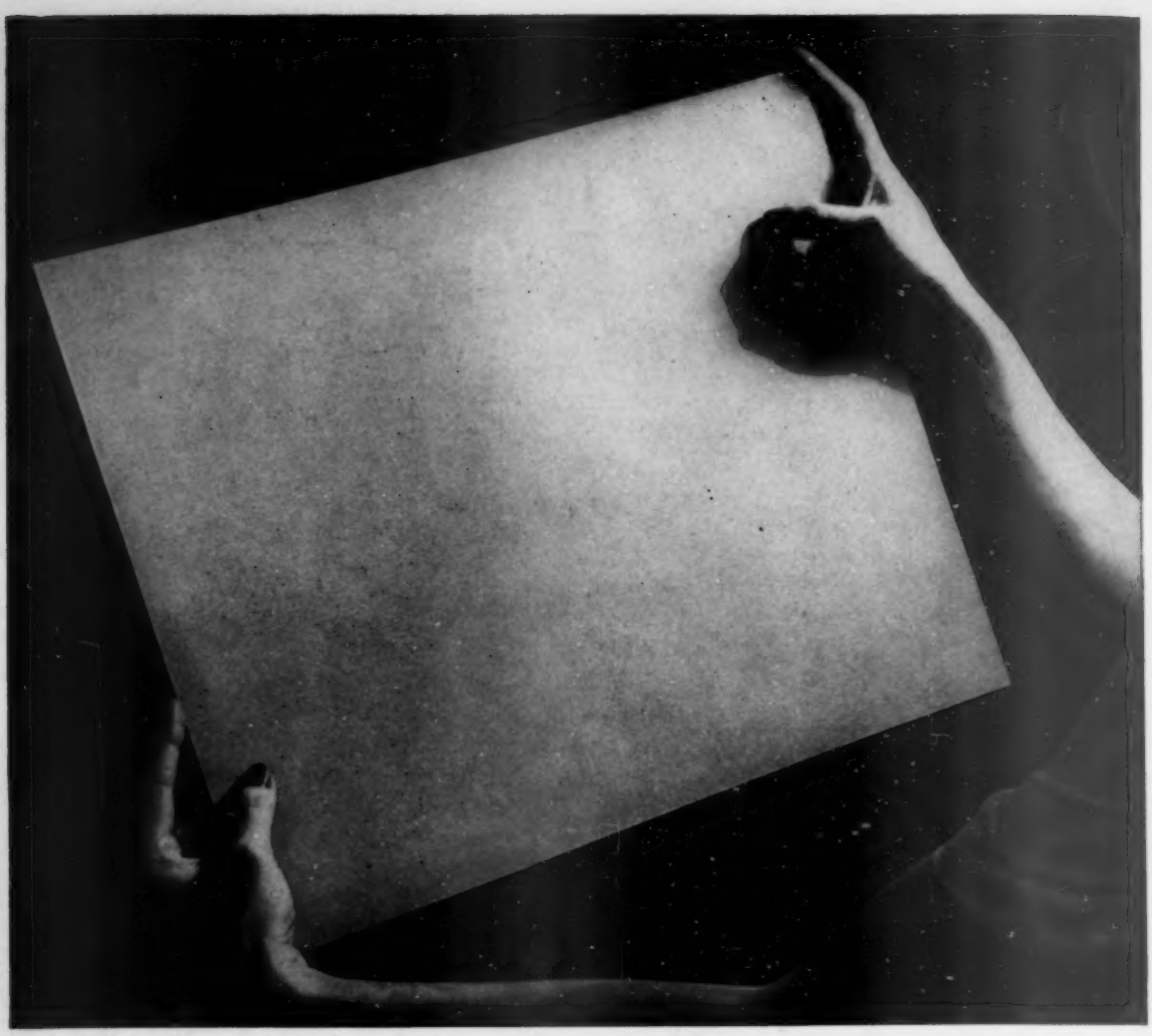

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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THE ROENTGEN SIGNS OF PATENT DUCTUS ARTERIOSUS

A SUMMARY OF 50 SURGICALLY VERIFIED CASES

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INTRODUCTION

THE first successful ligation of a patent ductus arteriosus was done by Gross[6] in 1938. The original suggestion for an operation to ligate this anomalous vessel was made by Munro[11] in 1907 but he did not attempt it on a living subject. O'Shaughnessy,[13] who was lost at the British evacuation from Dunkirk, had attempted ligation of a ductus arteriosus before Gross but in his case there had been an error in diagnosis and the ductus was found at operation to be already obliterated. Another prior attempt at ligation had been made by Strieder,[5] but for technical reasons the vessel could not be closed and the patient died suddenly on the fourth postoperative day.

A total of 50 cases of patent ductus arteriosus have now been ligated or divided by Gross, with 3 deaths. Seven of these patients had subacute bacterial endocarditis (*Streptococcus viridans* infection), this being such a frequent complication that we considered it best to include them in this study. All of the patients were studied preoperatively by roentgen methods and many of them postoperatively as well. Two additional patients were explored but the ductus was not ligated, since it was determined on exploration that some other congenital lesion was present in addition to patency of the ductus arteriosus. These 2 cases are not included in this report. This figure speaks for itself as to the accuracy of diagnosis before operation. Many articles and textbooks stress the point that congenital anomalies of the heart are apt to be multiple. Others give the opinion that patency of the ductus arteriosus may be a necessary shunt which, if obliterated, would result fatally. In this series of cases no such accident occurred, and in only 2 of the 52 cases operated on to date were there other cardiac anomalies.

The ages of the patients in the present series varied from eleven months to thirty-six years. The distribution between the sexes was 17 males and 33 females.

The ductus arteriosus or ductus Botalli is a short vessel connecting the aortic arch and the pulmonary artery (Fig. 1 and 2). It is a necessary part of the fetal circulation as it forms a by-pass around the pulmonary circulation. Thus blood leaving the right

ventricle during fetal life presumably enters the aorta directly from the pulmonary artery. Soon after birth the ductus normally closes. Its persistence beyond the first few weeks of postnatal life provides a shunt from the aorta, where the blood pressure is

FIG. 1. Schema of normal circulation. Unoxygenated blood is dark, arterial blood is white.

relatively high, into the pulmonary artery. This throws an extra quantity of blood into the lesser circulation and increases the work of the heart. Certain changes are thereby produced in the shape of the heart and in the dynamics of the circulation which are manifested in abnormal physical and roentgenographic signs. The latter will be discussed in detail.

The reasons for operating on a patient with a patent ductus arteriosus and the selection of cases for operation are subjects outside the scope of this discussion; they have been adequately presented in previous publications.[7,8,9] Suffice it to say that the results of a successful closure of the ductus are dramatic, in many cases converting a cardiac cripple into a normal individual, as shown by all clinical tests. This makes it most important that a correct diagnosis of this disorder be made so that the cases can be segregated from the general group of congenital heart disease. The suitability of a given case for operation can then be discussed on a rational basis. Accordingly we are presenting herein a summary of the roentgenologic findings in the first 50 cases of patency of the ductus arteriosus that have been treated by Gross, the diagnosis being thereby confirmed anatomically. This group includes the cases whose roentgen studies have been previously published by Gross[8] and by Eppinger and Burwell.[3]

A roentgen examination cannot establish a diagnosis of patent ductus arteriosus. Probably the most reliable single feature in the diagnosis is the recognition of the characteristic continuous "machinery" murmur by one who has examined a number of such patients. It should be remembered that a loud murmur is compatible with minimal evidence of heart disease by roentgen examination, because a loud murmur may be caused by a small ductus.

There are other confirmatory findings that should be looked for in a patient suspected of having a patent ductus arteriosus, especially a systolic thrill in the pulmonic area, or a thrill of maximum intensity during systole.[7] Roentgen studies are an important adjunct in the diagnosis and their value has been well stated by Eppinger and Burwell:[3] ". . . appropriate X-ray studies may (1) suggest the diagnosis, (2) contribute important confirmatory

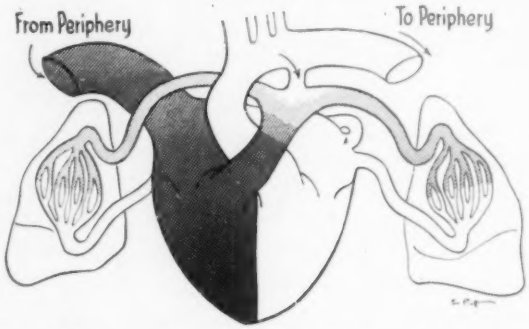

FIG. 2. Schema of abnormal circulation with patent ductus ateriosus. Note mixture of arterial (oxygenated) blood with venous (unoxygenated) blood in pulmonary artery, and recirculation of blood through left side of heart.

evidence, and (3) bear important witness as to the effectiveness of therapy." Their enlightening research will be referred to later.

Zinn[18] was probably the first to record the roentgen findings in a patient suspected of having a patent ductus, although the

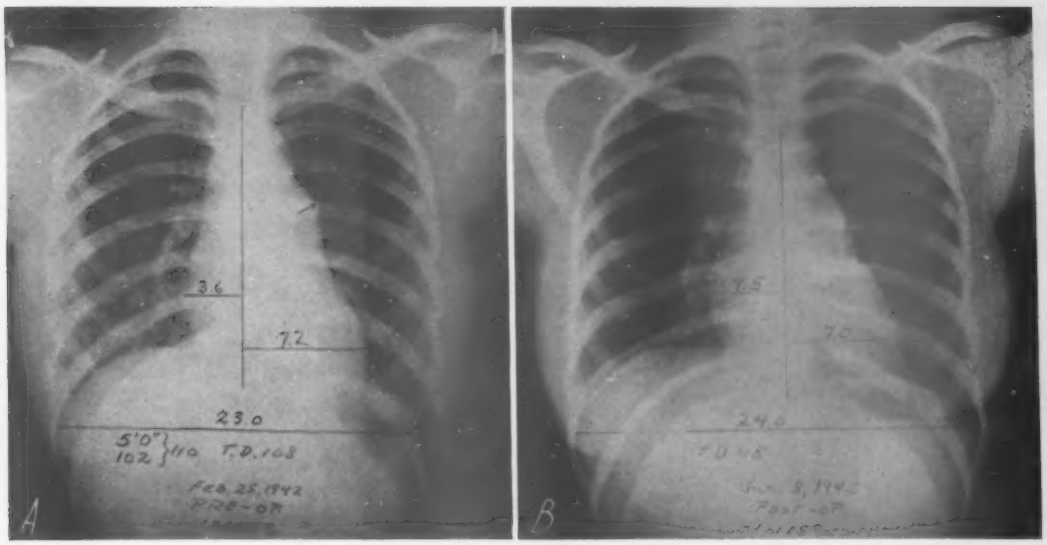

Fig. 3. Typical contour of heart in patient with patent ductus arteriosus before operation (*A*). Note prominent pulmonary artery just below aortic arch on left border and engorgement of pulmonary vessels. *B*, ten months after ligation of the ductus arteriosus. Note flattening of pulmonary artery shadow and decrease in size of pulmonary vessels. Heart is actually larger in size but the patient has grown taller and gained weight since operation (Case 34 in Table II).

examination had actually been made by Grunmach. The diagnosis in Zinn's case was not verified and may be considered doubtful since the patient had clubbed fingers. He presented a sketch outline of the heart in systole and in diastole and stressed the presence of a dilated, pulsating pulmonary artery. The location of this large pulmonary artery shadow agreed with the position of the maximal intensity of the murmur, which was said to be "a very loud systolic murmur extending into diastole." There was also a thrill in this region.

In later years dilatation of the pulmonary artery was repeatedly described as the explanation for an area of percussion dullness in the left first intercostal space called Gerhardt's dullness.

Hubeny[10] in 1920 reported a case of patent ductus arteriosus confirmed by autopsy, and he made a comprehensive review of the literature on the roentgen findings in this condition. Much of this consisted of single case reports, many of them with the diagnosis unproved. In general, there was agreement that an exaggerated beat of the left ventricle and of the pulmonary artery was the most important sign in the roentgen examination of these patients.

Explanation of Roentgen Signs

The roentgen signs to be looked for in a suspected case of patent ductus arteriosus are:

1. An enlarged left ventricle.
2. An enlarged left auricle.
3. A dilated pulmonary artery.
4. An exaggerated beat of the left ventricle and of the pulmonary artery.
5. "Hilar dance," or systolic expansion of the large vessels in the hila of the lungs.
6. Engorgement of the pulmonary vessels.

Not all of the patients will show all of these signs but one or several of them can be shown in practically every case. A combination of several of the above abnormalities should make one suspect the diagnosis.

The experimental work of Eppinger and Burwell[3,4] has given us a sound explanation for these signs. They analyzed samples of blood taken from the aorta and the pulmo-

nary artery in a number of Gross's cases during the operation for ductal closure. The flow of blood is from the aorta into the pulmonary artery, which accounts for the lack of cyanosis in these patients (Fig. 1 and 2). Their results, moreover, showed that, under the conditions of operation, from 45 to 75 per cent of the blood pumped out by the left ventricle passed back into the pulmonary artery by way of the ductus. In the cases studied the left ventricle had to pump from two to four times the amount of blood put out during the same time by the right ventricle. They have summarized the effects of these altered mechanics as follows:

a. The left ventricular enlargement is the result of its greatly increased output.

b. With each beat an increased volume of blood passes through the left ventricle and pulmonary artery causing an increased pulsation of these structures.

c. The prominence of the pulmonary artery is due to its receiving blood from both the right ventricle and the aorta.

d. The pulsation of the branches of the pulmonary artery, or "hilar dance," is accounted for by the increased inflow into the artery itself.

e. The extra volume of blood in the lesser circulation leads to vascular congestion and finally, "If a normal mitral valve is not wide enough to transmit this large amount of blood without an elevated left auricular pressure, there may be visible dilatation of the left auricle."

Table 1 is a summary of the frequency of the above signs in our series of 50 verified cases of patent ductus arteriosus.

TECHNIQUE OF EXAMINATION

As in all types of heart disease, roentgenoscopy is the most important part of the roentgen study. This should be done before taking roentgenograms as one can then best decide what special films should be made. Patients who are too weak to stand up for roentgenoscopy because of fever or long confinement to bed can be

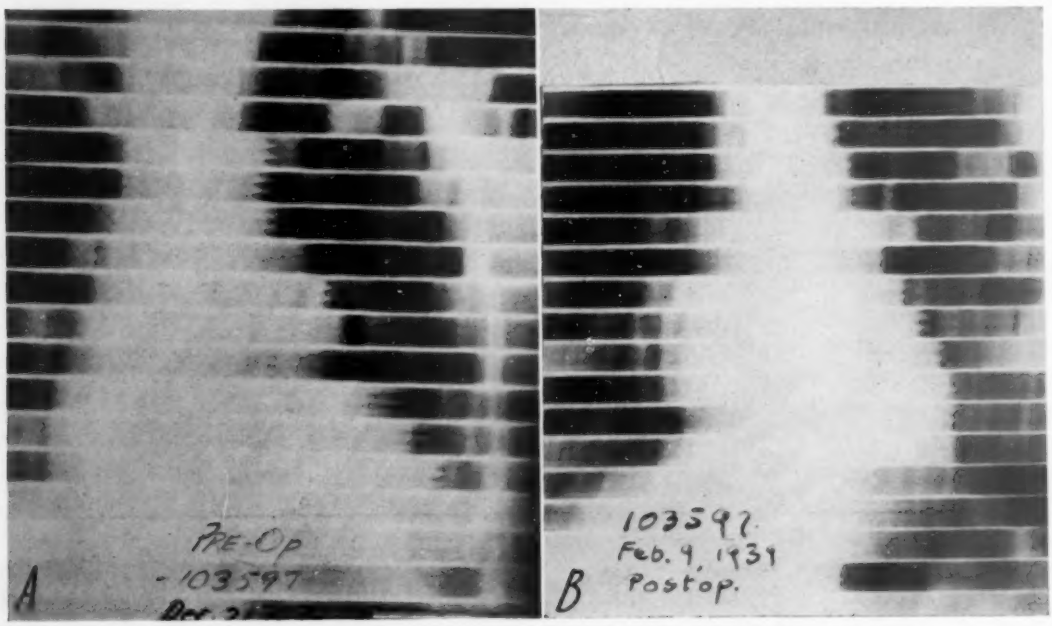

FIG. 4. Roentgen kymograms of patient with patent ductus arteriosus to demonstrate exaggerated pulsation of left ventricle, pulmonary artery, and aorta (*A*), and marked diminution of pulsations after ligation (*B*). Calculated blood flow in pulmonary circulation before ligation was 10.3 liters per minute, and in peripheral circulation 3.4 liters per minute. After ligation of the ductus arteriosus the calculated flow in both circuits was 4.0 liters per minute. (See Eppinger, Burwell and Gross[4].)

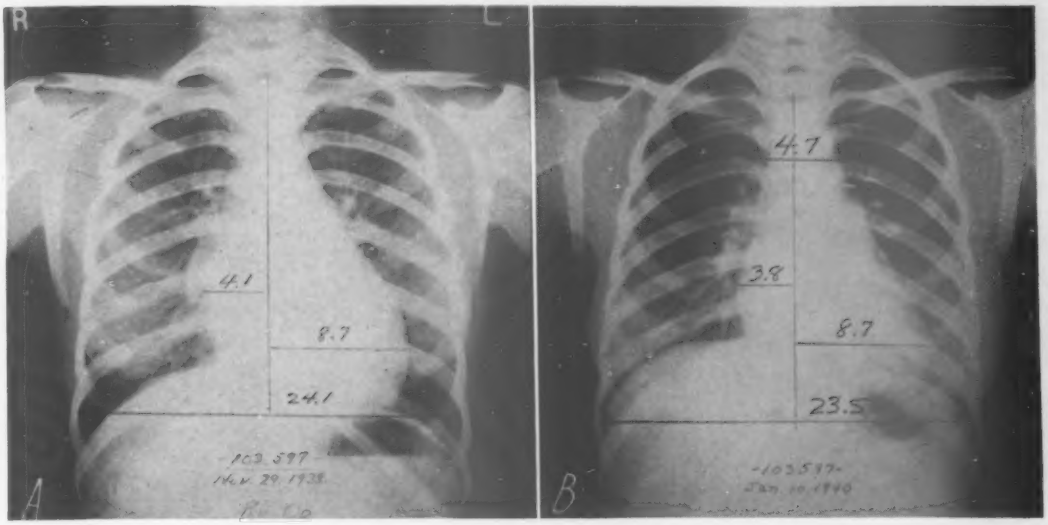

Fig. 5. Same patient as Figure 4. Frontal projection of heart before operation (*A*) and after ligation of the ductus arteriosus (*B*). Heart is slightly enlarged by cardiothoracic ratio. Although the transverse diameters are almost identical, there has obviously been a considerable decrease in heart volume after ligation.

placed on a stool the feet of which are mounted into a wooden frame fitted with casters beneath. They can then be wheeled from bed into the roentgenoscopic room, studied in all projections while they still sit on the stool, then wheeled into the roentgenographic room for films. These can, of course, be taken with the patient sitting. Many patients can sit erect on a stool for several minutes without fatigue who would be unable to stand long enough for a satisfactory examination.

The size, shape, and motion of all chambers of the heart should be closely observed, besides noting the type of rhythm. The latter was regular in all of our patients with patent ductus arteriosus and need not be mentioned further except to say that the heart rate is often increased.

After roentgenoscopy a teleroentgenogram should be taken in posteroanterior projection as well as roentgenograms in both left and right anterior oblique positions. In many cases we added a roentgen kymogram as this gives a record of the rate and amplitude of the cardiac pulsations. Postoperative kymograms were then found to be of value for comparison with the preoperative, giving graphic evidence of "the impressive contrast between the violently overactive left ventricle with the ductus open and the relatively calm left ventricle after ligation."[3]

In a few cases angiocardiograms were made as it was felt that this procedure might give additional aid in the diagnosis. It does not offer conclusive evidence but it is sometimes of help in ruling out other associated congenital lesions.

Roentgenological Findings

Cardiac Enlargement. Roesler[15] has already observed that large hearts are rare with patent ductus arteriosus and in our cases the largest hearts were seen in those with subacute bacterial endocarditis or endarteritis. The remainder had either no enlargement or only slight to moderate enlargement and in these the enlargement was limited to the left side of the heart. In most of our cases the estimation of cardiac enlargement was based on the cardiothoracic ratio, with a ratio of 0.5 or more probably indicating an enlarged heart. In Table II it will be seen that a few cases are marked "plus" under cardiac enlargement even though the cardiothoracic ratio is less than 0.5. This is because their roentgeno-

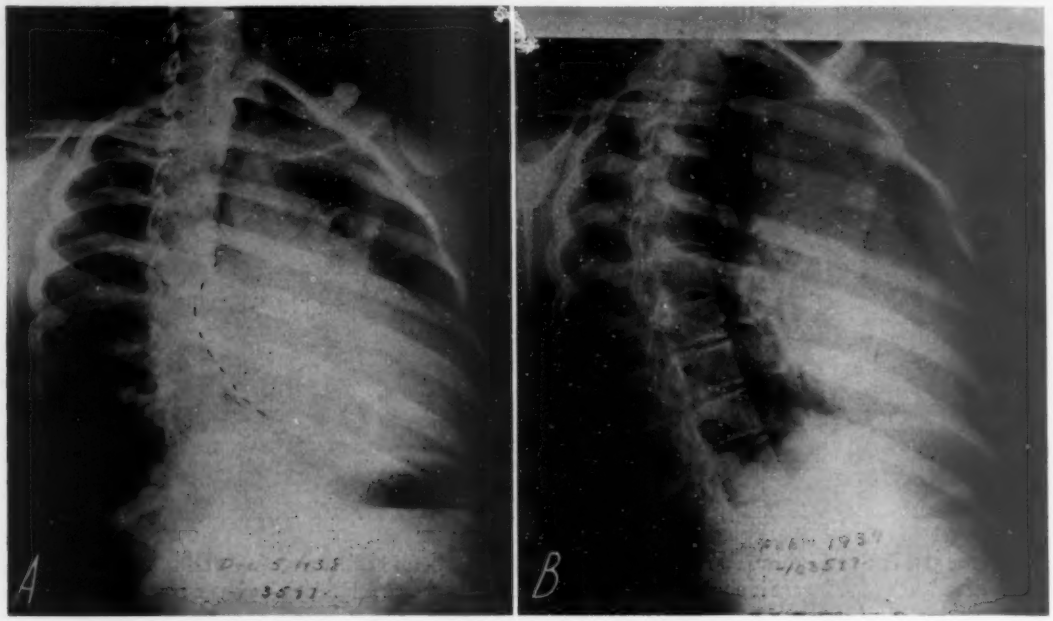

FIG. 6. Same patient as Figures 4 and 5. Right anterior oblique projections demonstrating fairly marked dilatation of the left auricle posteriorly on preoperative roentgenogram (*A*), and its diminution in size after ligation of the ductus arteriosus (*B*). (Case 4, Table II.)

grams gave a definite impression of enlargement of the heart due to a left auricular fullness on the left border, or to enlargement downward, or both. In other words, these were cases in which we were confident that an estimation of surface area would have shown enlargement even though the transverse diameter did not.

In the adults we now use a much more accurate method than the cardiothoracic ratio in deciding whether or not the heart is enlarged. This consists of the use of the table of theoretical normal transverse diameters published by Ungerleider and Clark.[17] This table has been worked out for adults only. It is the most trustworthy means of estimating minor degrees of enlargement. No computation is involved in the use of this method, one needs to know only the height and weight of the patient. Reference to the table then gives the predicted normal transverse diameter of the heart, and this figure is compared to the diameter measured on the roentgenogram. With an allowed variation of 10 per cent above the theoretical normal before considering the heart enlarged, we have found the table reliable and indispensable in our work. This height-weight table of cardiac diameters fulfills a criterion stressed by Comeau and White[2] in their discussion of methods of measuring heart size, in that it is a *prediction* table. That is, for a given set of body measurements the table predicts the normal average heart size.

Enlargement of the Left Auricle. A dilated left auricle is one of the commonest signs of a patent ductus arteriosus, being in our experience exceeded in frequency only by cardiac enlargement and enlargement of the pulmonary artery. This does not agree with Roesler's earlier statement.[15] The dilated auricle must be looked for in the right anterior oblique projection as a smooth, rounded bulge into the posterior mediastinal space (Fig. 6). If one is uncertain about its presence a swallow of barium sulfate suspension will be of help, as the lower third of the esophagus will usually be displaced posteriorly by a dilated left auricle. A roentgenogram should be taken in this projection too, but the roentgenoscopic examination

is all-important in deciding about this sign.

An enlarged left auricle is practically a constant finding in mitral stenosis but the differentiation of this condition from an open ductus arteriosus will rarely offer much difficulty to an experienced clinician. In quite a few instances these two lesions can be reliably separated on roentgenographic evidence alone. Of critical importance would be a search for a calcified valve or valves, in case both mitral and aortic valves are damaged. One of us[16] has found calcified valve leaflets to be indisputable evidence of rheumatic heart disease. None of our patients with patent ductus arteriosus showed intracardiac calcifications which were large enough or dense enough to be seen with the roentgenoscope. Additional evidence for rheumatic heart disease would be the presence of auricular fibrillation, if that were found, rather than the regular rhythm which is seen in the uncomplicated patency of the ductus arteriosus.

Dilatation of the Pulmonary Artery. An enlarged pulmonary artery is one of the most frequent signs of congenital heart disease and it was present in the majority of our cases. Sometimes this enlargement can be better appreciated on a right anterior oblique projection, which casts into relief the true pulmonary conus. This structure is not visible on a posteroanterior film, the prominence often called pulmonary conus being actually the pulmonary artery.

Here, again, a marked enlargement is seldom seen unless there are vegetations of bacterial endarteritis on the wall of the artery. A very large pulmonary artery, especially if combined with a fairly marked or extreme enlargement of the heart, is apt to be due to a combination of congenital anomalies such as tetralogy of Fallot (combined overriding aorta, right ventricular hypertrophy, interventricular septal defect, and pulmonary stenosis), or Eisenmenger's complex (similar to the tetralogy of Fallot except that there is pulmonary artery dilatation rather than stenosis), or to interauricular septal defect. The last condition may have an associated mitral stenosis and insufficiency, the combination being called Lutembacher's syndrome. In many of these patients with more severe congenital heart disease one can demonstrate enlargement of the right ventricle, by an elevation of the apex of the heart or by a prominence along the anterior border of the heart in the left anterior oblique view. Right ventricular enlargement was not demonstrable in any of our cases of patent ductus, which coincides with Gross's statement that in childhood, at least, the presence of right

TABLE I

A SUMMARY OF THE FINDINGS IN 50 CASES OF PATENT DUCTUS ARTERIOSUS

	Present	Absent	Not Recorded	Questionable	Total Recorded (Present plus absent plus questionable)	Per Cent Positive
Dilated pulmonary artery	41	8	0	1	50	82
Cardiac enlargement	38	12	0	0	50	76
Enlarged left auricle	32	11	5	2	45	71
Engorgement of pulmonary vessels	35	12	0	3	50	70
Exaggerated beat of left ventricle and pulmonary artery	28	13	9	0	41	68
"Hilar dance"	13	22	13	2	37	35

TABLE II

COMPLETE SUMMARY OF THE PATIENTS WITH PATENT DUCTUS ARTERIOSUS OPERATED UPON AND THEIR ROENTGEN FINDINGS

+ = definitely present
++ = a moderately prominent feature
+++ = an unusually prominent feature
o = not present
NR = not recorded
± = uncertain or questionable

Patient	Sex	Age	Cardiac Enlargement	Enlargement of Left Ventricle	Dilatation of Left Auricle	Enlargement of Pulmonary Artery	Increased Pulsation of Left Ventricle and Pulmonary Artery	"Hilar Dance"	Engorgement of Pulmonary Vessels	Heart Size (in millimeters)		Postoperative Pleural Fluid	Postoperative Elevation of Diaphragm
										Before operation	After operation		
1. L.S.	F	7½	++	++	++	++	++	++	+++	heart 117 / chest 200	107 / 225	+	o
2. R.C.	M	11	+	++	+	+	o	o	+	113 / 213	120 / 227	+	o
3. F.S.	F	7	++	++	+	++	++	++	++	97 / 190	88 / 186	+	o
4. M.F.	F	17	+ (15%)	++	++	+	+++	o	+	128 / 241	121 / 243	++	o
5. D.M.	F	11½	++	++	++	+	+	+	+	120 / 217	112 / 210	o	o
6. C.L.	F	6	+	+	NR	++	+	NR	++	98 / 182		++	o
7. L.B.	F	15	++	++	++	o	++	o	+++	109 / 193		+++	NR
8. D.S.	F	5	+	++	+	+	NR	NR	+	100 / 176	90 / 166	o	o
9. M.S.	F	26	+ (10%)	+	+	++	+	+	+	137 / 246	137 / 248	++	++
10. J.M.	F	8	+	++	+	++	+	o	+	106 / 210		++	o
11. C.S.	M	2	+	++	NR	+	++	NR	+	96 / 158	88 / 162	o	+
12. D.D.	M	7	++	+++	+	+	++	o	+	128 / 214		o	o
13. H.B.	F	6	+	+	+	+	+	o	o	98 / 184		o	o
14. K.K.	F	22	+	+	+	+	+	+	+	123 / 246		NR	o
15. S.K.	F	24	+	+	o	++	NR	NR	±	129 / 272	128 / 265	NR	+
16. W.H.	M	10½	+	+	+	++	o	o	o	116 / 228	117 / 250	o	+
17. A.P.	F	6	++	++	+	o	+	+	+	100 / 180	95 / 176	++	o
18. B.V.	F	4½	+++	+++	++	+++	++	o	+++	114 / 184		+++	NR
19. W.N.	M	25	o	+	++	++	NR	o	++	125 / 282	129 / 284	+	o
20. M.L.	F	10	+	+	+	+	+	o	o	111 / 220	103 / 202	+++	o
21. F.R.	M	9½	+	++	±	++	+	+	++	105 / 197		+	o
22. H.O.	M	12½	++	+	±	++	NR	NR	++	124 / 240		+	o
23. R.M.	M	3	++	++	+	++	+	NR	+++	93 / 165	87 / 176	+	o
24. G.G.	M	11	+	+	+	+	NR	NR	±	120 / 243		+++	o
25 A.F.	M	10	o	+	+	+	NR	NR	±	94 / 186	85 / 172	NR	NR

TABLE II (*continued*)

+ =definitely present
++ =a moderately prominent feature
+++ =an unusually prominent feature
o =not present
NR =not recorded
± =uncertain or questionable

Patient	Sex	Age	Cardiac Enlargement	Enlargement of Left Ventricle	Dilatation of Left Auricle	Enlargement of Pulmonary Artery	Increased Pulsation of Left Ventricle and Pulmonary Artery	"Hilar Dance"	Engorgement of Pulmonary Vessels	Heart Size		Postoperative Pleural Fluid	Postoperative Elevation of Diaphragm
										Before operation (in millimeters)	After operation		
26. M.C.	F	7½	+	++	+	+	+	o	++	94/173	91/193	o	o
27. G.T.	M	31	o	o	NR	o	NR	NR	+	127/300		++	+
28. E.N.	F	8	o	o	NR	o	NR	NR	+	95/207		+	o
29. C.A.	F	6½	+++	+++	+	++	+	+	++	117/191	95/195	NR	NR
30. E.B.	F	13	o	o	o	++	o	o	o	98/245	102/233	++	o
31. J.K.	M	12½	++	++	o	++	+	+	+	112/220	125/239	++	NR
32 P.M.	M	12	++	++	+	+	++	+	++	123/80		NR	NR
33. C.W.	F	1	+	++	NR	+	o	NR	++	220/130		o	o
34. R.L.	F	20	o	o	+	+++	++	o	+	110/230	117/240	NR	NR
35. D.V.	F	10	++	++	o	+++	o	o	++	117/200	110/219	+++	NR
36. B.L.	M	35	++ (25%)	++	+	+	o	+	+	155/317	155/318	NR	NR
37. M.F.	F	30	+ (10%)	+	o	+	o	o	o	116/235		+	o
38. N.F.	F	16	+ (10%)	+	+	+	o	o	+	122/250	132/240	+	o
39. I.R.	F	15	+ (15%)	++	+	o	+++	±	++	123/251		o	o
40. B.N.	F	13	o	o	+	+	+	o	o	112/247		+	+
41. M.H.	F	6	o	o	o	o	NR	NR	o	87/178		+++	NR
42. N.A.	F	4½	++	++	+	+	o	o	+	92/158		++	o
43. E.M.	M	12	+	+	o	o	++	+	o	113/220		++	o
44. J.V.	F	15	+++ (40%)	++	++	+	o	NR	+++	144/248		++	o
45. C.P.	M	21	+ (11%)	++	++	+	+	±	o	147/293		+	o
46. M.B.	F	19	o (+6%)	o	o	+	++	o	o	122/271	114/280	++	+
47. S.R.	F	36	o (+7%)	o	o	+	o	o	o	121/249	117/242	+	o
48. M.R.	F	6	+	++	++	±	o	o	++	104/188		+	o
49. B.B.	M	6	o	o	o	o	o	o	o	95/201	93/196	o	o
50. S.B.	F	24	o	+	o	+	+	+	+	117/268	115/250	+	o

axis deviation in the electrocardiogram should make one suspicious of some other cardiac abnormality.

For further evidence in differentiating patency of the ductus arteriosus from the above group of congenital heart diseases we must rely on the clinical and electrocardiographic findings. The presence of cyanosis and a different type and location of murmur and thrill should make one doubt the existence of a patent ductus as the only anomaly. Interventricular septal defect, for example, frequently causes a bundle branch block or even heart block.

Increased Pulsation of the Left Ventricle and Pulmonary Artery. Accentuated pulsation of the left ventricle and the pulmonary artery was seen in about two-thirds of the cases (Table 1). It is shown to good advantage in Figure 4. The pulsation of the pulmonary artery occurs synchronously with the ventricular contraction, being due to the rush of blood into it from the right ventricle and the aorta.

The importance of this sign alone makes us appreciate that a roentgenoscopic study is mandatory in the roentgen diagnosis of heart disease. A kymogram is never an adequate substitute for roentgenoscopy because of its serious limitations. The kymogram shows the motion of the heart along two borders only; it records the horizontal motion of the heart borders but not the vertical component, so that the depth of the waves on the tracing omits the contraction of the heart along its long (oblique) axis, which often makes up much of the heart's contraction. The exaggerated pulsation or increased amplitude of the left ventricular excursion is common to several diseases or conditions. Chief among these are the increased excursions noted in hyperthyroidism, in marked anemia, in aortic insufficiency, in recent pneumothorax, and in arteriovenous aneurysm. The heart beat in hyperthyroidism has a peculiar "jittery" character and all chambers and both large vessels share in it. The rate is increased in hyperthyroidism and also in anemia, with both conditions presenting roentgenoscopic evidence of increased work of the heart, both in rate and in output per beat. In aortic insufficiency the heart beat has a distinctive rocking character, with quick expansion and collapse, particularly of the aorta. This corresponds to the collapsing or "Corrigan" pulse felt at the wrist. In arteriovenous aneurysm essentially the same mechanism is present as in patent ductus arteriosus, an abnormal communication between a large artery and a large vein. The characteristic pulsation in patent ductus is the exaggerated systolic pulsation of the aorta and pulmonary artery occurring simultaneously with the exaggerated ventricular contraction. In peripheral arteriovenous aneurysm the aorta pulsates abnormally with the left ventricular beat but the pulmonary artery shows a normal amplitude of pulsation.

Hilar Dance. One further sign should be looked for during roentgenoscopy: the "hilar dance" or pulsating hilar vessels. This was present in approximately one-third of the cases in which a search for it was made. It may be seen in other congenital heart lesions, so its presence is in no way diagnostic of a patent ductus arteriosus nor does its absence rule it out. However, it is well to bear it in mind and to look for it closely.

Engorgement of Intrapulmonary Vessels. This was most marked in the 7 patients who had bacterial endocarditis or endarteritis. In others, it is apt to be a minor feature. Sometimes its presence could be considered definite only when we had a postoperative roentgenogram to compare with the preoperative, showing the diminution in size of the vascular shadows in the lungs after ligation of the ductus.

Angiocardiography. The visualization of the great vessels and cardiac chambers by roentgen examination after the injection of a radiopaque substance into the venous system is now a well established accessory method for the study of abnormalities of the cardiovascular system.

In this series angiocardiographic studies were carried out in 5 cases. In each case in-

formation of value was obtained but in no instance have we been able to visualize the ductus arteriosus. Barclay and his associates,[1] working with sheep fetus, have made repeated attempts to visualize the patent ductus but in all instances have been unsuccessful except after retrograde injection into the aorta. The complexity of dense shadows obscures the ductus. It is possible to obtain excellent visualization of the enlarged chambers and of the dilated pulmonary vessels. Most important of all is the evidence of recirculation of the dye through the pulmonary vessels as shown by the continued opacification of the pulmonary artery and to a lesser extent of the left ventricle. This in conjunction with the findings which have been elaborated upon tend to confirm the diagnosis, but it appears to be doubtful whether by angiocardiography alone a definite diagnosis of patency of the ductus arteriosus could be made.

In general, the technique employed has been that of Robb and Steinberg[14] although we have used a special semi-automatic cassette changer.[12]

POSTOPERATIVE COMPLICATIONS

After operation there is usually some effusion into the left pleural space, which is necessarily opened during the operation. In our patients this occurred in 33 out of 43 cases in which roentgenograms were made during the first few weeks following the operation. The amount of fluid varied from a small collection in the costophrenic sulcus to a large effusion filling most of the left hemithorax and displacing the heart to the opposite side. However, in all instances but one this was spontaneously absorbed in from two to four weeks. The exception was a patient who developed an encapsulated empyema in the left upper chest. After a catheter drainage was instituted she made a satisfactory recovery.

Another complication, which was less frequent, was a temporary paralysis of the left hemidiaphragm, presumably due to trauma to the left phrenic nerve. This occurred in 7 cases out of 40 in which a record was made. It is apt to disappear within a month, although one patient still had a slightly elevated left hemidiaphragm two

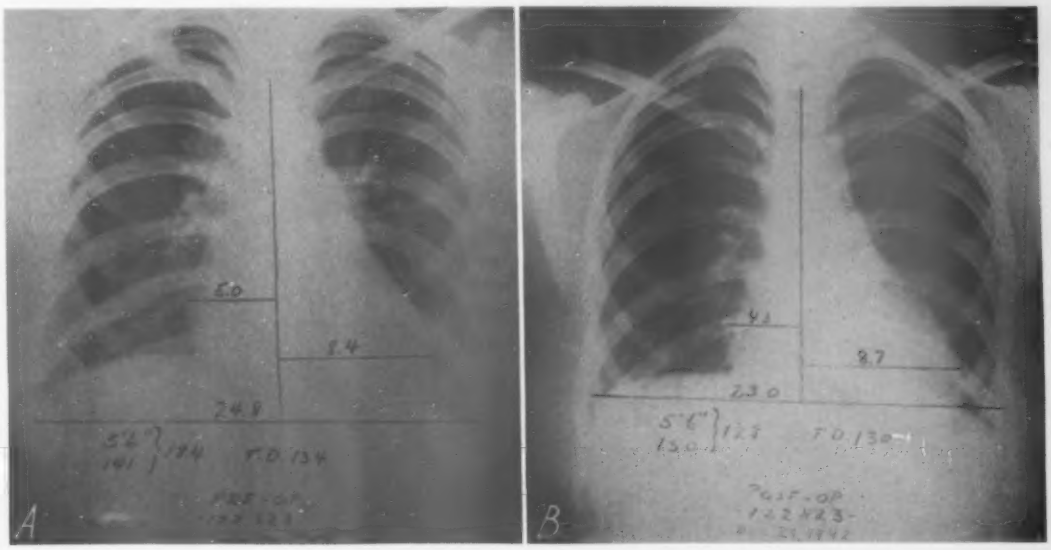

Fig. 7. Frontal projections, roentgenograms taken at 7 ft. distance, before and after ligation of a patent ductus arteriosus. Very little change in size or shape of the heart, but a marked decrease in size of the hilar vessels after ligation (*B*). (Case 38, Table II.) See Figure 8 for oblique views.

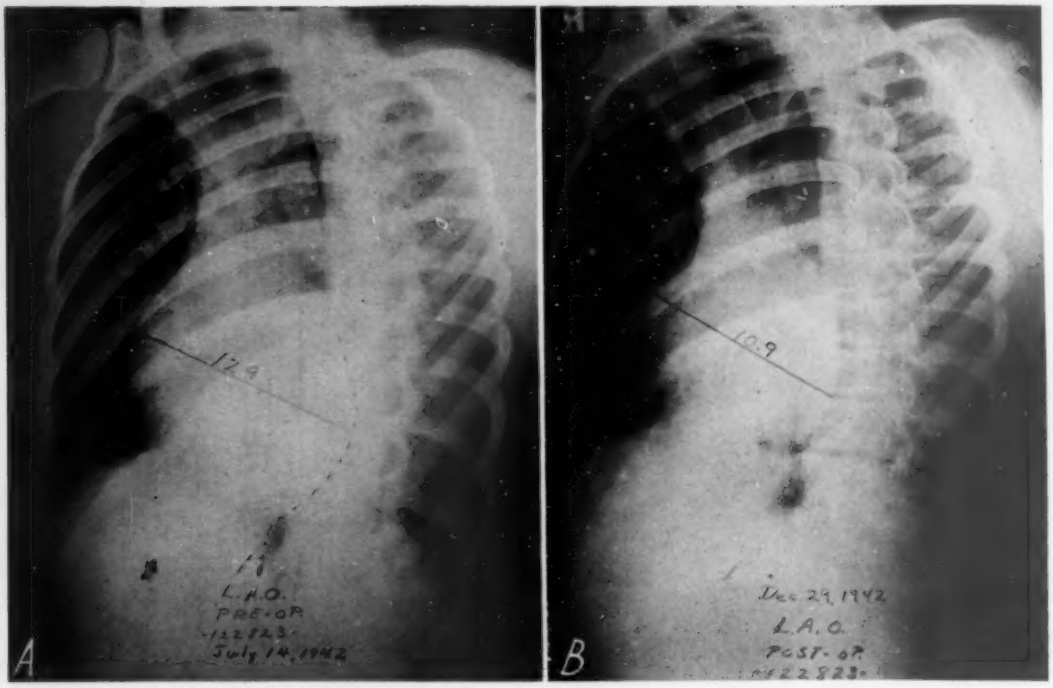

FIG. 8. Same patient as Figure 7; left anterior oblique projections. Note marked decrease in maximal diameter of the heart in this view after ligation. *A*, before operation; *B*, after operation. The two silver clips formerly placed on the ends of the ligatures show clearly in *B* just above the left main bronchus.

years and four months after operation. At that time each leaf of the diaphragm moved 3 centimeters under roentgenoscopic observation.

One patient developed what is apparently a false aneurysm around the ligated ductus arteriosus. This was seen as a large, rounded, pulsating mass adjacent to the pulmonary artery, and the silver clips which had been placed on the ends of the ligatures were found widely separated. On subsequent examinations the mass has decreased slightly in size.

CHANGES RESULTING FROM CLOSURE OF THE DUCTUS ARTERIOSUS

Roentgenoscopy and kymograms after closure of the ductus will show a reduction of the ventricular pulsation to the normal amplitude, the pulmonary artery no longer enlarged and pulsating, hilar dance absent, and the left auricle will either be reduced in size or normal. On roentgenograms one often detects a reduction in size of the intrapulmonary vessels. This may be most noticeable in the hilar and perihilar areas of the lungs.

Contrary to what we might expect, there is seldom a marked decrease in the transverse diameter of the heart on postoperative roentgenograms. The actual data in our series are as follows: Out of 27 cases in which an accurate heart measurement could be made following operation, 13 hearts decreased in transverse diameter by 5 mm. or more; 10 were considered unchanged, as the diameter was altered 4 mm. or less; 4 increased in size by 5 mm. or more. This failure of many patients to show a clear cut decrease in heart diameter seems out of keeping with the immediate restoration of the blood pressure to normal and the abolition of the murmur and thrill. It can perhaps be considered a result of the absence of marked cardiac enlargement while the ductus is open. In Case 38 there was a rather striking decrease in heart size in the left anterior oblique projection (Fig.

8). We suspect, therefore, that accurate measurements of heart volume, if they were possible, would show a smaller heart after operation more regularly than we can demonstrate it by comparing transverse diameters.

With children it often seems that the patient "grows up to" the increased size of the heart. When these younger patients are examined one or two years after their operation the heart will be found to be of normal, or nearly normal, size for the larger chest resulting from growth.

SUMMARY

1. A patent ductus arteriosus can now be safely ligated or completely divided, which places this congenital lesion among the curable forms of heart disease.

2. The accurate diagnosis of this condition is now vastly more important than formerly, when it was chiefly of academic interest. The roentgenologic signs of patency of the ductus arteriosus have a definite value, although they do not prove the diagnosis, nor does their absence rule it out. In addition, a thorough roentgen study helps the surgeon evaluate the results of operation.

3. The roentgen findings in 50 cases of patent ductus arteriosus which were verified by operation are presented. These findings in order of frequency are: (a) dilatation of the pulmonary artery; (b) cardiac enlargement; (c) dilatation of the left auricle; (d) engorgement of the intrapulmonary vessels; (e) exaggerated pulsation of the left ventricle and the pulmonary artery; (f) "hilar dance," or pulsation of the vessels in the hila of the lungs.

We are indebted to Dr. Philip Avery, Middlesex General Hospital, New Brunswick, N. J., for postoperative roentgenograms on Case 34, and to Dr. Robert Reeves, Duke Hospital, Durham, N. C., for postoperative roentgenograms on Case 36.

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ANGIOCARDIOGRAPHY IN CONGENITAL HEART DISEASE

III. PATENT DUCTUS ARTERIOSUS*

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ONE of the most outstanding of recent advances in the therapy of heart disease is the successful surgical ligation of patent ductus arteriosus. This was first accomplished by Gross[5] in 1938. Subsequently the operation has been performed successfully by Touroff[12] in instances of patent ductus arteriosus with superimposed subacute bacterial endarteritis. The clinical diagnosis of this congenital lesion rests largely upon the presence of the characteristic to-and-fro machinery murmur and thrill over the pulmonic area. However, it is generally agreed that this finding is not present in all instances, especially in infancy and early childhood. The roentgen appearance of the heart, while helpful, is not pathognomonic. Obviously it would be highly desirable to establish the diagnosis of this congenital anomaly beyond reasonable doubt in order better to establish the indication for surgical intervention.

Twenty-seven cases of patent ductus arteriosus have been studied by means of angiocardiography. The method employed was the rapid intravenous injection of 70 per cent diodrast solution (Winthrop) as described by Robb and Steinberg.[6] The position of choice for the roentgen examination was found to be the left anterior oblique, 50 to 70 degrees. The first two cases of this series were recorded by the multiple exposure fluorographic technique;[9] the remainder by serial roentgen films employing a rapid film changer.[10] Complete clinical, cardiographic and conventional roentgenologic studies of each patient preceded angiocardiography.

ANATOMICAL CONSIDERATIONS

Patent ductus arteriosus may occur in association with numerous other congenital cardiac malformations. Such cases rarely live beyond infancy. Occasionally the ductus arteriosus remains patent as a compensatory mechanism in the presence of stenosis of the pulmonic trunk, with or without patency of the interventricular septum. Hence, it may be found in association with the tetralogy of Fallot. These cases may live to adult life but are easily distinguished from "isolated" patent ductus arteriosus by the presence of constant cyanosis. More often, the condition occurs as a single lesion, the remainder of the heart being completely normal. These cases reach adult life and constitute the group which were studied.

Anatomical descriptions of patent ductus arteriosus uniformly represent it as a funnel-shaped structure. Sternberg[8] stated that "the ductus is funnel-shaped at its aortic end in every instance, diminishing progressively in diameter as it approaches the pulmonary artery." The diameter of the ductus varies considerably, ranging from 2 mm. to more than 1 cm. The diameter at the aortic end is usually two to three times that of the pulmonic end. Another constant anatomical feature of patent ductus arteriosus is its shortness. The majority of recorded cases are no longer than 1 cm.

An important associated anatomical effect of patent ductus arteriosus was described by Thoma[11] in 1890 under the title of "Traction Aneurysm of the Aorta in Childhood in the Presence of Patent Ductus

* Grateful acknowledgment is made to the Winthrop Chemical Company for the donation of the diodrast solution 70 per cent which was used in this study.

† Fellow of the Dazian Foundation for Medical Research.

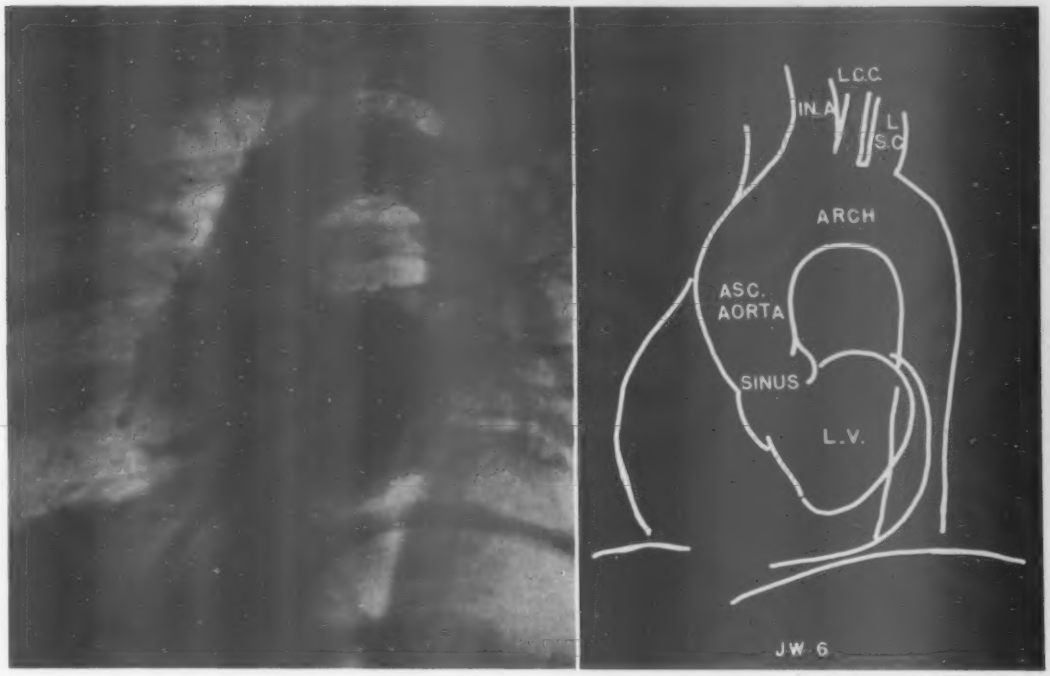

FIG. 1. Normal boy, aged fourteen. Left anterior oblique position. The aorta shows a normal smooth curve. The lumen is uniform in the arch and proximal descendens.

Arteriosus." A localized dilatation of the descending aorta was found at the origin of the ductus (Fig. 4). Histopathological studies proved that this was not an aneurysm of the ductus. Re-examination of Rokitansky's[7] previously reported cases showed each to have a similar aortic dilatation. Thoma felt that this resulted from a traction effect produced by the short ductus. He suggested also that a similar dilatation might occur occasionally at the pulmonic artery on the same basis. Maude Abbott[1] described dilatation of the pulmonic artery to be present invariably. Vierordt,[13] on the other hand, stated that both the cardiac chambers as well as the pulmonic artery could occasionally be entirely normal.

PHYSIOLOGICAL CONSIDERATIONS

The direction of blood flow in circulatory shunts is determined by the existence of a pressure gradient. Because cyanosis is absent in these cases and in view of the normally higher pressure within the aorta, it is assumed that blood flows from the aorta to the pulmonary artery. Objective proof of this assumption is available at operation of such patients since the blood in the pulmonary artery has been found to contain more oxygen than the blood in the right ventricle.[4] This definitely indicates that arterial blood has entered the pulmonary artery via the ductus. Reversal of flow with appearance of cyanosis is an extreme rarity. To compensate for the amount of blood lost from the systemic circulation the stroke volume of the left ventricle is necessarily increased in order to maintain peripheral blood flow. This may result in hypertrophy and dilatation of the left ventricle. The degree to which this actually occurs may be considered as an indication of the amount of stroke volume increase required and is presumably proportional to the amount of shunt. It is very likely that the latter is related to the size of the ductus. Eppinger and his co-workers[4] have calculated that the volume of blood shunted from aorta to pulmonary artery in 3 oper-

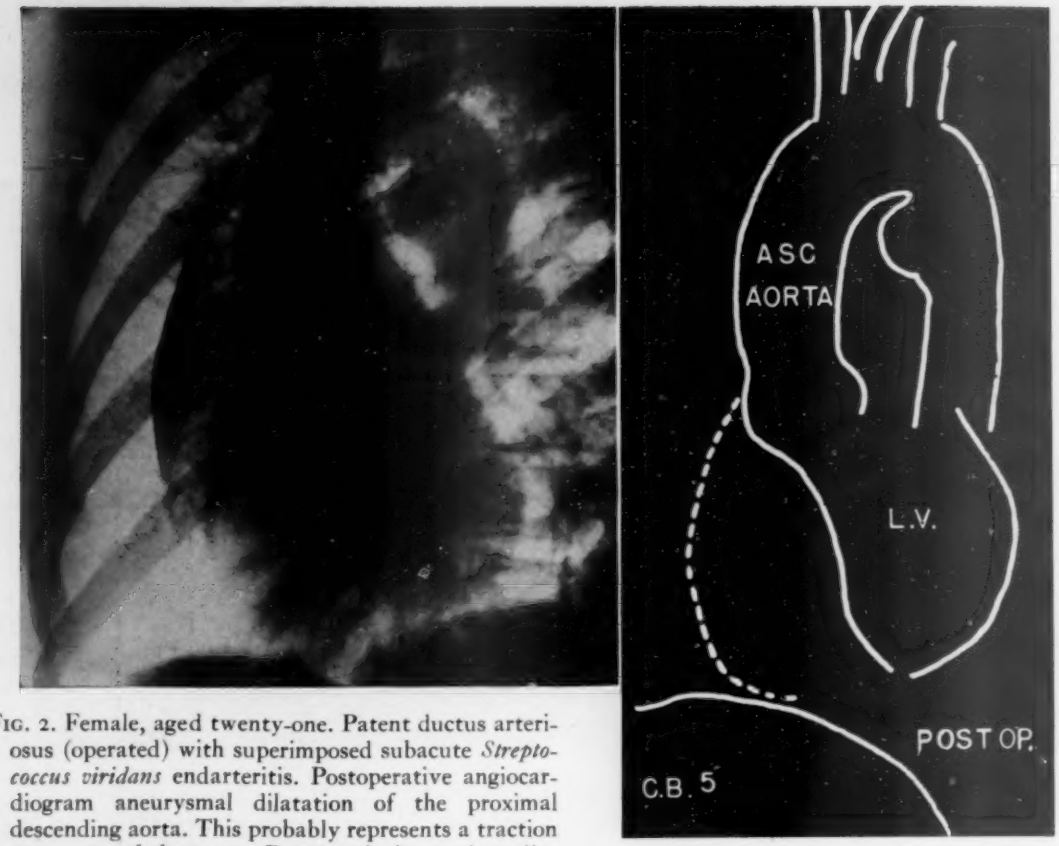

FIG. 2. Female, aged twenty-one. Patent ductus arteriosus (operated) with superimposed subacute *Streptococcus viridans* endarteritis. Postoperative angiocardiogram aneurysmal dilatation of the proximal descending aorta. This probably represents a traction aneurysm of the aorta. Preoperatively, angiocardiogram showed a more diffuse dilatation.

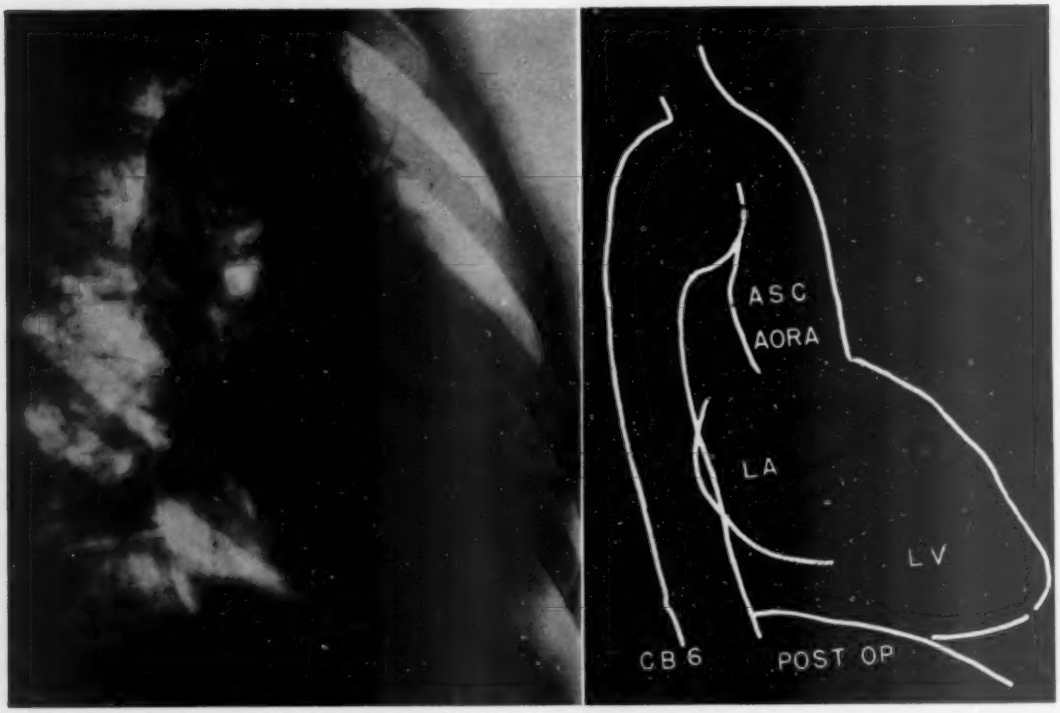

FIG. 3. Same case as Figure 2. Right anterior oblique position. Traction aneurysm at origin of patent ductus is seen.

ated cases in which the ductus measured 7 to 9 mm. in diameter was between 45 and 77 per cent of the stroke volume of the left ventricle. The low mean pressure and high pulse pressure frequently encountered in patent ductus arteriosus are the expression of the high stroke volume and the diminished peripheral resistance. The blood volume also is increased. These circulatory adjustments reflect an attempt at compensation, and will vary in individual instances with the severity of the lesion.

ANGIOCARDIOGRAPHIC FINDINGS

In the left anterior oblique position the normal pulmonary artery and its main branches and the aorta are visualized in a more or less constant relation and pattern (Fig. 1).

In patent ductus arteriosus the following deviations from the normal have been observed: (1) A distinct localized dilatation of the descending aorta just beyond the isthmus. A small bulge or a more or less uniformly dilated segment may be seen. The projection varies in size but is constant in its direction toward the main and left pulmonary arteries (Fig. 2, 3 and 5). Although best seen in the left anterior oblique position it has also been demonstrated in the left lateral and in the right anterior oblique positions. In the latter, it becomes superimposed on the descending aorta but may be differentiated with little difficulty. The appearance is comparable with the experimental data published by Barclay, Barcroft, Barron and Franklin.[2] These investigators studied the circulation in fetal sheep using contrast media and serial cineroentgenograms. The location and appearance of the patent ductus arteriosus on retrograde aortic injection in fetal sheep is identical with that seen in our cases. (2) An elevation of the main and left pulmonary arteries, the appearance suggesting that they are drawn towards the isthmus of the aorta. (3) Dilatation of the main and major branch pulmonary arteries. (4) Varying degrees of left ventricular dilatation.

Incidence of Findings. Of the 27 cases of patent ductus arteriosus studied angiocardiographically, 26 showed the aortic abnormality described above. Twelve of these cases were proved at operation. Of the latter, 8 were examined preoperatively and 4 only postoperatively; 3 were studied both pre- and postoperatively. Three operated cases in which silver clips were placed on the ductal ligatures in situ by Drs. A. S. W. Touroff and E. E. Arnheim demonstrated these to be in the exact location of the aortic dilatation.

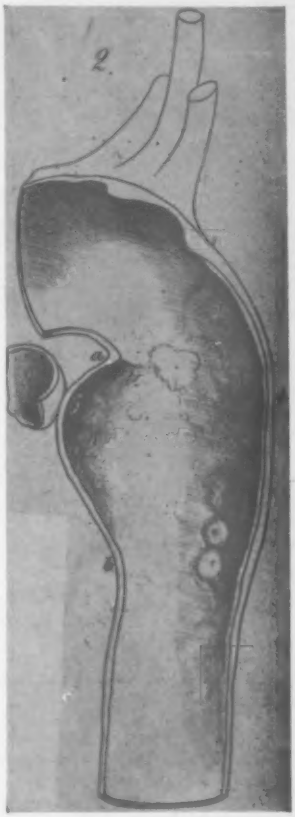

Fig. 4. Traction aneurysm of aorta in a case of patent ductus arteriosus shown at postmortem (copied from Thoma, 1890).

The pulmonary artery, particularly in the region of the bifurcation, was elevated to some degree in all instances studied. The caliber of the pulmonary artery varied as follows: normal, 6 cases; moderate dilatation, 13 cases, and marked dilatation 8 cases. Varying degrees of left ventricular dilatation were present in 18 cases. The left ventricle was of normal size in 9 cases.

TABLE I

Case	Age yr.	Sex	Cardiac Lesion Discovered at Age of	Symptoms	Physical Findings	Clinical Complications	Blood Pressure	Electrocardiogram
1 R.H.	9	M	8 yr.	None	No thrill over pulmonic area	None	92/52	Peculiar axis deviation. QRS_{123} diphasic; T_1 semi-inverted
2 A.F.	9	M	6 mo.	Physical underdevelopment; frequent bronchopneumonia	No thrill over pulmonic area	*Strep. viridans* bacteriemia, 2 yr. previously	80/26	No abnormality
3 R.K.	28	F	3 yr.	Occasional dyspnea on exertion	Systolic thrill over pulmonic area	None	138/80	No abnormality
4 H.S.	30	M	1½ yr.	No symptoms before onset of subacute bacterial endarteritis (*Streptococcus viridans*)	Continuous thrill over pulmonic area	*Strep. viridans* endarteritis—1 yr.	132/70	Left axis deviation
5 E.M.	25	F	25 yr.	Occasional dyspnea and chest pain	Systolic thrill over pulmonic area	None	115/70	Tendency to right axis deviation. QRS_{123} diphasic
6 E.F.	21	F	12 yr.	Palpitation and dyspnea; mental retardation	Systolic thrill over pulmonic area	None	100/58	Tendency to right axis deviation. Q_{123} diphasic
7 B.R.	10	M	10 yr.	Physical development retarded	Continuous thrill over pulmonic area	*Strep. viridans* endarteritis—4 mo.	114/64	No abnormality
8 G.G.	11	M	3 yr.	Frequent pneumonia	Systolic thrill over pulmonic area	None	102/52; after exercise 132/28	Marked left axis deviation
9 J.K.	18	F	10 yr.	Dyspnea and fatigue on exertion; mental retardation	No thrill; prominent pulsations over pulmonic area	None	134/84	Right axis deviation, prominent P waves, PR interval measured 0.22 sec.
10 R.W.	12	F	7 yr.	Slight dyspnea on exertion	Continuous thrill over pulmonic area	None	120/80; after exercise 128/43	No abnormality
11 M.B.	32	F	30 yr.	Dyspnea on exertion; easy fatigability	No thrill	None	106/58	QRS measured 0.10 sec.
12 T.O'S.	19	M	7 yr.	Asymptomatic	No thrill	None	126/76	No abnormality
13 J.M.	7	M	6 yr.	Occasional dyspnea	No thrill	None	100/60	Peculiar axis deviation, QRS_{123} diphasic
14 H.N.	9	M	8 mo.	Occasional dyspnea on exertion	Continuous thrill over pulmonic area	*Strep. viridans* endarteritis—2 mo.	115/52; after exercise 120/40; postop. 114/88	No abnormality
15 E.C.	9	M	6 yr.	Dyspnea on exertion	No thrill; prominent pulsations over pulmonic area	None	98/62	Right axis deviation, QRS_{123} diphasic
16 O.R.	12	F	11 yr.	Asymptomatic	Continuous thrill over pulmonic area	None	90/60	Tendency to right axis deviation
17 C.B.	20	F	5 yr.	Asymptomatic before onset of subacute bacterial endarteritis (*Streptococcus viridans*)	Continuous thrill over pulmonic area	*Strep. viridans* endarteritis—6 wk.	134/54; postop. 110/80	Tendency to right axis deviation, QRS slurred

TABLE I

Phonocardiogram	Roentgen Examination of Heart		Angiocardiography				Operation	Size of Ductus Arteriosus	Remarks
			Pulmonary artery		Left ventricle	Dilatation of aorta beyond isthmus			
	Size	Configuration	Size	Elevation					
Systolic murmur and faint early diastolic murmur over pulmonic area	+++	Prominent pulmonic artery segment	+++	+++	+++	Slight			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	Normal	Slight prominence of pulmonic artery segment	+	++	+	Slight	Ligation by Dr. R. E. Gross	"Very short"	Disappearance of murmurs postoperatively. Blood pressure, 96/76
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	+	Slight prominence of pulmonic artery segment	+	++	++	Localized bulge			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	Normal	Prominent pulmonic artery segment	++	+++	Normal	Localized bulge	Ligation by Dr. A. S. W. Touroff; silver clips	Diameter $\frac{1}{8}$ in.; length $\frac{3}{4}$ in.	Persistent short systolic murmur. No change in electrocardiogram or roentgen findings postoperatively
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	Normal	Prominent pulmonic artery segment	+	++	Normal	Localized bulge			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	Normal	Prominent pulmonic artery segment	++	++	+	Fusiform			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Slight prominence of pulmonic artery segment	Normal	+	+	Slight			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Prominent pulmonic artery segment	+	+++	++	Fusiform	Ligation by Dr. R. E. Gross		
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Prominent pulmonary artery segment	Normal	++	+	Localized bulge			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	Normal	Prominent pulmonary artery segment	Normal	++	Normal	Slight			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	+	Prominent pulmonary artery segment	+	+	+	Slight			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Pulmonic artery not prominent	+	+	++	Localized bulge			
Systolic and very short early diastolic murmurs over pulmonic area. Systolic over jugular notch	Normal	Left pulmonic artery slightly dilated	+	+	+	Normal			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Prominent pulmonic artery segment	+	++	++	Localized bulge	Ligation by Dr. A. S. W. Touroff	Diameter $\frac{1}{8}$ in., length $\frac{1}{2}$ in.	Persistent short systolic murmur; no change in electrocardiogram or roentgen findings postoperatively
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	+	Prominent pulmonic artery segment	++	++	+	Localized bulge			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	Normal	Prominent pulmonic artery segment	+	+	+	Slight			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Pulmonic artery not prominent	Normal	+	++	Localized bulge	Ligation by Dr. A. S. W. Touroff	Diameter $\frac{1}{8}$ in., length $\frac{1}{2}$ in.	Persistent faint systolic murmur. No axis deviation postoperatively; accentuation of aortic bulge postoperatively

TABLE I—*Continued*

Case	Age yr.	Sex	Cardiac Lesion Discovered at Age of	Symptoms	Physical Findings	Clinical Complications	Blood Pressure	Electrocardiogram
18 M.G.	6	F	3 wk.	Asymptomatic	Continuous thrill over entire precordium and neck; pallor	None	104/46	Marked right axis deviation. QRS of very high voltage
19 N.F.	16	F	1 wk.	Occasional dyspnea on exertion	Systolic pulsation over pulmonic area; no thrill	None	122/52; after exercise 142/42	Tendency to right axis deviation. Q_2 and Q_3
20 I.A.	33	M	1 mo.	Dyspnea on exertion and palpitation before onset of subacute bacterial endarteritis (*Strep. viridans*)	No thrill; development of aortic insufficiency murmur and Corrigan pulse, while under observation	*Strep. viridans* endarteritis—4 mo.	116/50; postop. 136/70	Left axis deviation Q_1 and Q_2. QRS slurred and notched
21 E.S.	3	M	3 yr.	Asymptomatic	No thrill	None	84/48	No abnormality
22 J.D.	11	F	3½ yr.	Occasional dyspnea on exertion	Continuous thrill over entire precordium	None	112/68; after exercise 126/52	No abnormality
23 F.S.*	29	F	8 yr.	Asymptomatic before onset of subacute bacterial endarteritis (*Strep. viridans*)	Continuous thrill over pulmonic area	*Strep. viridans* endarteritis—10 days before operation	Preop. 114/60; postop. 154/96	No abnormality preop.; left axis deviation postop.
24 S.S.*	29	F	Birth	Asymptomatic before onset of subacute bacterial endarteritis (*Strep. viridans*)	Continuous thrill over pulmonic area	*Strep. viridans* endarteritis—2½ mo. before operation	Preop. 108/68; postop. 110/70	Left axis deviation; no change postop.
25 G.O.*	51	F	22 yr.	*Strep. viridans* endarteritis with spontaneous recovery 12½ yr. previously; symptoms of cardiac failure	Continuous thrill over pulmonic area, disappeared postoperatively	*Strep. viridans* endarteritis—4 wk. before operation	Preop. 105/60; postop. 134–86	Left axis deviation postop.
26 P.H.	10	F	9 yr.	Asymptomatic before onset of acute bacterial endarteritis (*Staph. aureus*)	Continuous thrill over pulmonic area, disappeared postoperatively	Acute bacterial endarteritis 11 days before operation	Preop. 100/48; postop. 108/60	Tendency to right axis deviation
27 J.Z.*	18	F	1½ yr.	Physical and mental retardation; dyspnea on exertion	Continuous thrill over pulmonic area, disappeared postoperatively	*Strep. viridans* endarteritis—3 mo. before operation	Preop. 102/46; postop. 98/60	No axis deviation postop. T_1 semi-inverted, T_2 low

Cases are arranged in chronological order of angiocardiographic studies.
* These cases have been reported in detail by Touroff, Vesell and Chasnoff.[12]

Discussion. It was expected that the shunt of blood from the aorta to the pulmonary artery would result in continuous visualization of the pulmonary vascular tree since the pressure in the aorta is much higher than that in the pulmonary artery. If the data reported by Eppinger and his co-workers on the percentage of stroke volume of the shunt in ductus arteriosus be accepted one would expect a distinct revisualization of the pulmonary vascular tree. However, it seems unlikely that such high figures as even 50 per cent of the stroke volume could be reached in the usual case. These investigators recognized many possible sources of error, the most serious being the assumption that the blood drawn from the left pulmonary artery at the hilum of the lung represented a complete mixture of venous and shunted arterial blood. In the human, a higher oxygen saturation would be expected in this artery since the ductus enters to the left of the bifurcation. In a few of our cases, there did indeed appear to be a slight but distinct persistence of the opacification. However, the dilution of the contrast medium when it is shunted into the pulmonary artery is so great that the slight variations in opacity are no greater than the density differences

TABLE I—*Continued*

Phonocardiogram	Roentgen Examination of Heart		Angiocardiography				Operation	Size of Ductus Arteriosus	Remarks
			Pulmonary artery		Left ventricle	Dilatation of aorta beyond isthmus			
	Size	Configuration	Size	Elevation					
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Prominent pulmonic artery segment	+	+	++	Fusiform dilatation			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	++	Pulmonic artery not prominent	Normal	+	++	Fusiform dilatation			
Systolic and early diastolic murmurs best heard over Erb's area radiating to neck	+	Pulmonic artery not prominent	+	+	++	Fusiform dilatation	Ligation by Dr. A. S. W. Touroff	Diameter $\frac{1}{4}$ in., length $\frac{1}{4}$ in.	No change in murmurs, electrocardiogram or roentgen findings postop.; probably aortic valve involved by subacute bacterial endarteritis
Systolic murmur loudest over Erb's area	Normal	Pulmonic artery not prominent	Normal	+	Normal	Small localized bulge			
Systolic and diastolic murmurs of machinery type over pulmonic area. Systolic over jugular notch	Normal	Markedly prominent pulmonic artery segment	+	++	Normal	Fusiform dilatation	Ligation by Dr. E. E. Arnheim; silver clips	Diameter $\frac{1}{4}$ in., length $\frac{3}{4}$ in.	Disappearance of murmurs; no change in electrocardiogram or roentgen finding postop.
Continuous machinery murmur preop. Short early systolic over pulmonic area, postop.	+	Pulmonary artery segment very prominent	++	+	Normal	Localized bulge	Ligation by Dr. A. S. W. Touroff	Diameter $\frac{1}{4}$ in., length $\frac{1}{4}$ in.	Postop. angiocardiographic studies only
Continuous machinery murmur preop. which persisted unchanged after operation	Normal	Prominent pulmonic artery segment	+	+	Normal	Localized bulge	Ligation and section of ductus by Dr. A. S. W. Touroff	Diameter $\frac{3}{8}$ in., length $\frac{3}{8}$ in.	Postop. angiocardiographic studies only; persistence of murmurs and thrill
Continuous machinery murmur preop., short early systolic murmur postop.	++	Prominent pulmonic artery segment	++	+	+	Slight	Ligation by Dr. A. S. W. Touroff	Diameter $\frac{1}{4}$ in., length $\frac{1}{4}$ in.	Postop. angiocardiographic studies only
Systolic and diastolic murmurs of machinery type preop.; short early systolic murmur postop.	++	Prominent pulmonic artery segment	++	+	++	Fusiform dilatation	Ligation by Dr. A. S. W. Touroff; silver clips	Diameter $\frac{1}{4}$ in., length $\frac{1}{4}$ in.	
Systolic and diastolic murmurs of machinery type preop.; short early systolic murmur postop.	+++	Marked prominence of pulmonic artery segment	+	+	++	Localized bulge	Ligation and section of ductus by Dr. A. S. W. Touroff	Diameter $\frac{1}{4}$ in., length $\frac{1}{4}$ in.	Postop. angiocardiographic studies only

which may be present in all roentgenograms. This finding must therefore be interpreted with considerable caution.

The aortic abnormality which was found in practically all of the cases studied in this series has not been seen by us in any condition other than patent ductus arteriosus. It is therefore probably characteristic of this condition. From the review of the anatomical features presented above, it would appear that the structure visualized may represent either the ductus itself since it is invariably funnel shaped, the aneurysmal aortic dilatation described by Thoma or a combination of these two. In any individual case it would be impossible to determine which is present. The persistence of the aortic dilatation after operation might be interpreted as indicating the presence of a traction aneurysm. In one case, the dilatation appeared exaggerated postoperatively, possibly because the ductal obliteration resulted in greater shortening of the duct and therefore greater traction.

Another abnormality almost uniformly found in this group of cases and not encountered elsewhere is the unusual course of the pulmonary artery and its branches. Due to the shortness of the ductus, the pulmonary artery appears to be drawn upward toward the aortic isthmus thus obliterating part of the "aortic window." This differs

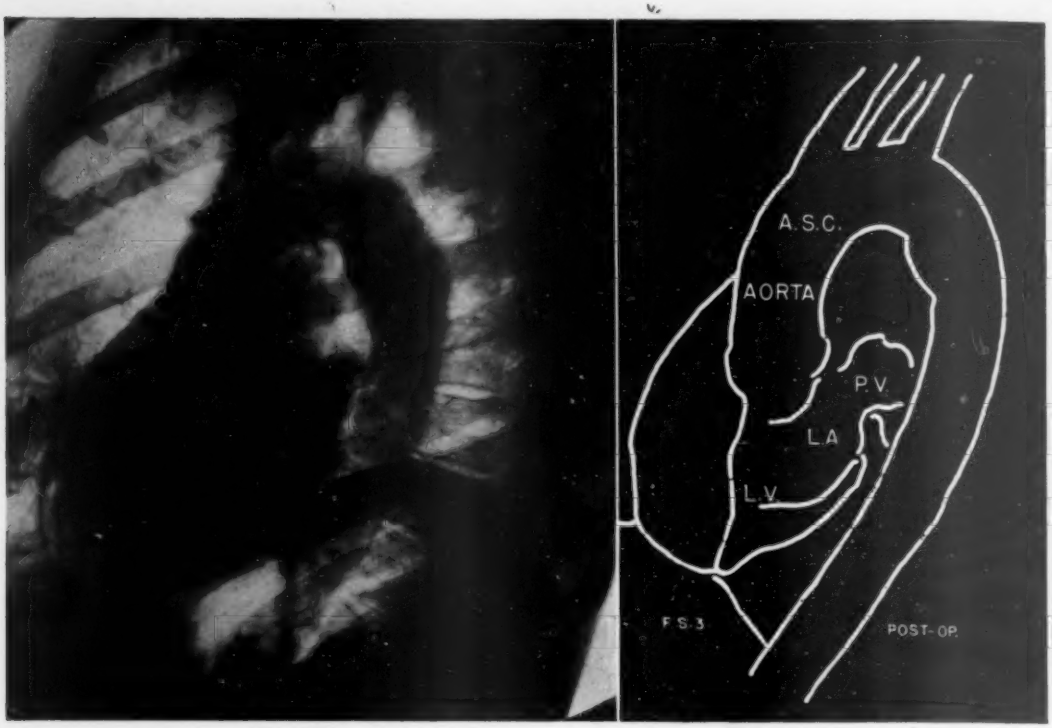

FIG. 5. Fusiform dilatation of proximal descending aorta in a case of patent ductus arteriosus. This probably represents the infundibulum of the ductus.

from the effect of the enlarged left auricle in mitral stenosis which displaces the pulmonary artery anteriorly as well as upwards, resulting in a smooth wide curve.

Heretofore, it has been assumed that the pulmonary artery is usually dilated in patent ductus arteriosus. This has been based on the assumption that prominence of the pulmonary artery segment in the conventional roentgenogram indicates dilatation of the pulmonary artery. This is not justified because elevation of the pulmonary artery may by itself account for this appearance as appeared in 6 cases of the present series.

Enlargement of the left auricle was not observed by us either on roentgenoscopic examination with a barium-filled esophagus or in the angiocardiograms. This is contrary to the experience of Eppinger and Burwell.[3] The problem is complicated because posterior displacement of the esophagus may be due to dilatation of the pulmonary artery or dilatation of the left ventricle as well as left auricular enlargement. When due to the artery, the esophageal displacement is in the region of the tracheal bifurcation just above the usual site of the left auricular displacement. When the esophageal displacement is due to left ventricular enlargement, on the other hand, it occurs at a lower level, often down to the diaphragm.

DIFFERENTIAL DIAGNOSIS

Congenital lesions which, in our experience, have been mistakenly diagnosed as patent ductus arteriosus are:

1. Interatrial septal defect
2. Idiopathic dilatation of pulmonary artery
3. Eisenmenger's complex
4. Pulmonic valve insufficiency due to absence of a cusp

These conditions have one common feature—an enlarged pulmonary artery. Since these conditions may be complicated by the presence of subacute bacterial endocarditis,

the need for accurate differentiation from patent ductus arteriosus is apparent, the latter being surgically remediable. A to-and-fro machinery murmur and thrill over the pulmonic area, identical with that heard in patent ductus, was present in one case; postmortem examination revealed absence of one of the pulmonic valve cusps causing pulmonary insufficiency, with superimposed subacute bacterial endocarditis. A patent ductus arteriosus was not present. In the other cases, the murmurs heard were either systolic or diastolic but were not of the machinery type.

In our experience, the aortic abnormality described with elevation of the pulmonary artery was found only in patent ductus arteriosus. While additional experience may provide exceptions, it is obvious that the angiocardiographic findings are of considerable value in the differentiation.

SUMMARY AND CONCLUSIONS

Angiocardiography in cases of isolated patent ductus arteriosus reveal:

1. A distinct localized dilatation of the descending aorta just beyond the isthmus which varies in size and shape from a localized bulge to a uniformly dilated segment. The appearance may be due either to the infundibulum of the patent ductus or perhaps in some cases to a traction aneurysm of the aorta.

2. An elevation of the main and left pulmonary arteries, the appearance suggesting that they are drawn toward the isthmus of the aorta.

3. Moderate to marked dilatation of the pulmonary artery usually was found. It was absent in 25 per cent of the cases.

4. Varying degrees of left ventricular dilatation.

In 27 cases of patent ductus arteriosus (12 of which were proved at operation) 26 showed the aortic abnormality described above.

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A CORRELATION BETWEEN THE ROENTGENOGRAPHIC CHANGES IN THE LUNGS IN LEFT VENTRICULAR FAILURE AND THE CIRCULATION RATES*

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THE roentgenographic appearance of the lungs in congestive heart failure is due primarily to the surplus of blood in the pulmonary circulation because of left ventricular failure. As the volume of blood confined to the lungs increases, the rate of blood flow from the right to the left side of the heart is retarded, resulting in prolongation of the systemic circulation time. This may be determined by measuring the arm-to-tongue circulation time by the saccharin method or the arm-to-carotid sinus time by the magnesium sulfate technique.[1,4,6]

Prominence of the hilar shadows has been associated with pulmonary congestion.[3,10,12,13] However, no definite information is available about a correlation between circulation rates and the roentgenographic changes in the lungs associated with heart failure. In order to study this point 20 patients with organic heart

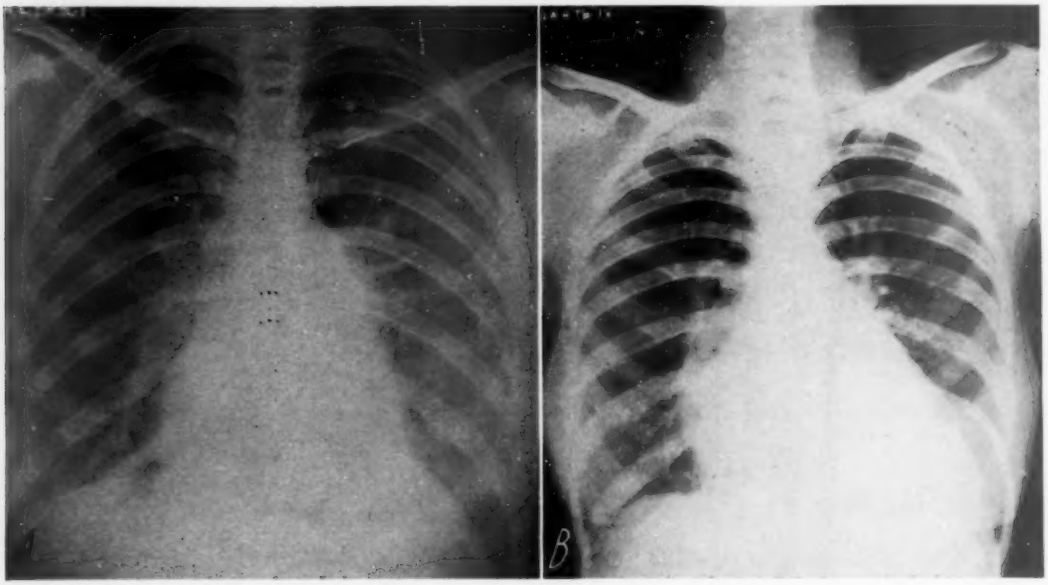

FIG. 1*A*. Teleroentgenogram of a female, aged twenty-seven, with mitral stenosis taken during her first episode of pulmonary edema which occurred during the sixth month of gestation. The patient had known of her cardiac condition for several years. The right lung root shows the haze seen with acute pulmonary congestion; the left hilum is obscured by the prominent pulmonary artery and right ventricle conus. The magnesium sulfate circulation time was twenty-one seconds, the ether time six seconds.

FIG. 1*B*. Teleroentgenogram of a female, aged forty, with mitral and aortic stenosis and insufficiency. The patient was comfortable when at rest. There had been several espisodes of congestive heart failure. The congestive changes at the right lung root are chronic, and less than might be expected. The left lung root is obscured by the left heart border. The magnesium sulfate circulation time was thirty-five seconds, the ether time twelve seconds.

* From the Radiologic Service of M. G. Wasch, M.D., The Jewish Hospital of Brooklyn.

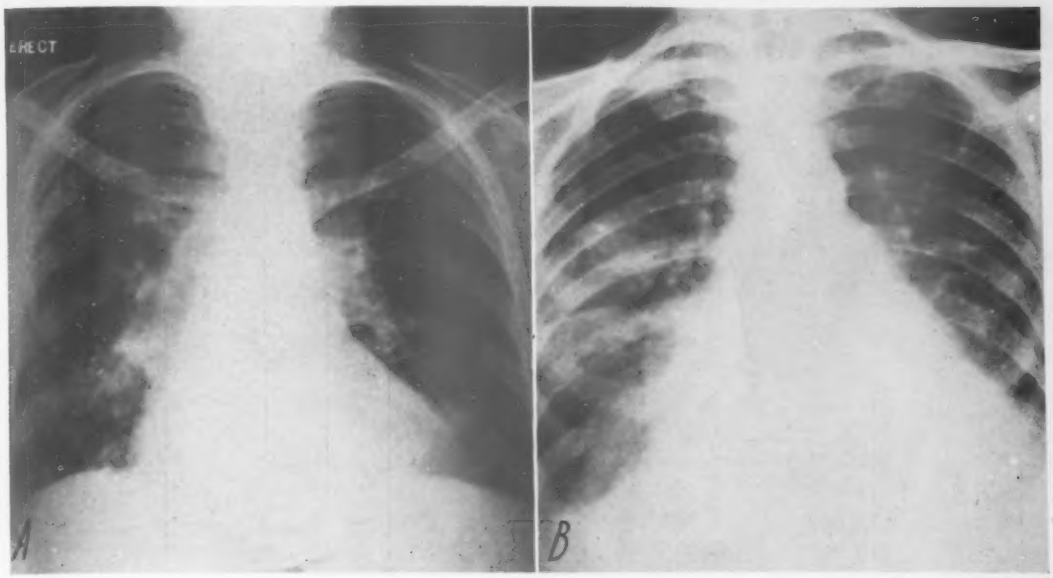

Fig. 2*A*. Teleroentgenogram of a male, aged fifty-five, with hypertensive and coronary artery heart disease. The patient was in chronic left ventricular failure when this roentgenogram was taken. He was relatively comfortable when at rest but became dyspneic on slight exertion. The congestive changes can be seen in both lung roots because the second left cardiac arc does not obscure the left hilum. His magnesium sulfate time was 27.4 seconds, ether time was eight seconds.

Fig. 2*B*. Teleroentgenogram of a female, aged fifty-two, with double mitral and aortic valve disease. The roentgenogram shows congestive changes at the right lung root and right paracardiac border as well as an interlobar effusion in the right midlung field between the upper and lower lobes. The magnesium sulfate time was 26.4 seconds, ether time was 9.7 seconds. The findings were confirmed at postmortem examination.

disease who were well compensated and 20 others in various phases of heart failure were studied from this aspect.

The roentgenologic studies and circulation rate determinations were made on the same day or one day apart. The normal values accepted for the saccharin time were between nine and sixteen seconds, and between seven and eighteen seconds for the magnesium sulfate time. In addition the arm-to-lung circulation rates were determined using the direct method of Moritz and Tabora.[9] Four to eight seconds were considered normal for the ether time[5] and values as high as 150 millimeters of water were considered normal venous pressures.

OBSERVATIONS

The 20 patients who were well compensated had had no previous episodes of heart failure. Their lung roots presented clear delination of the hilar arteries and the separations into secondary and tertiary branches were distinct. In most instances the shadows of the right pulmonary veins in the paracardiac region were visible. The circulation times were within normal limits in 18 of these patients. The other 2 patients with prolonged arm-to-tongue circulation rates had had mitral stenosis for a long time. Although neither had any clinical or roentgenographic evidences of heart failure they may have had pulmonary vascular changes undetectable at the time of roentgen examination. Such vascular changes have been mentioned by Parker and Weiss,[11] who described intimal thickening of the pulmonary arteries and hyperplastic arteriolar sclerosis secondary to mitral stenosis. The prolongation of the systemic circulation rates probably was due to this process in the latter 2 patients.

The other 20 patients had roentgenographic signs interpreted as due to con-

TABLE I

CASES WITH NO ROENTGEN EVIDENCE OF PULMONARY CONGESTION

Case	Diagnosis (Heart disease)	Valvular Disease	Age	Sex	$MgSO_4$ Time (sec.)	Saccharin Time (sec.)	Ether Time (sec.)	Venous Pressure (mm. H_2O)	Remarks
1	Rheumatic	Mitral insufficiency	15	F	9.0		6.5	100	
2	Rheumatic	Mitral insufficiency	15	F	12.0		6.0	105	
3	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	18	M	11.6		5.0	81	
4	Congenital	Interauricular septal defect. Mitral stenosis	35	F	13.4		4.0	131	
5	Rheumatic	Mitral insufficiency and stenosis	30	F		15.0	6.2	50	
6	Hypertensive		50	M	15.4		5.8	128	
7	Rheumatic	Mitral stenosis	36	F		16.4	6.4	86	Long standing mitral stenosis
8	Arteriosclerotic		57	M	12.4.		5.8	65	
9	Rheumatic	Mitral insufficiency and stenosis	13	M	13.0		8.2	50	
10	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency	10	M	10.0		6.5	70	
11	Hypertensive		53	M	15.0		7.9	113	
12	Rheumatic	Mitral insufficiency and stenosis	8	M	15.0		9.0	80	
13	Congenital	Interventricular septal defect	16	F	5.0		6.1	108	
14	Hypertensive; arteriosclerotic		65	F	14.8		9.0	104	
15	Pulmonic		36	M		13.0	9.0	150	
16	Congenital	Patent ductus arteriosus	8	F	9.0		4.9	110	
17	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency	50	F	37.7		11.0	153	Long standing mitral stenosis
18	Congenital	Interauricular septal defect	12	M	11.4		6.2	92	
19	Arteriosclerotic	Calcific aortic stenosis	47	M	15.6		5.5	108	
20	Hypertensive chronic glomerulonephritis		15	F		12.0	7.0	122	

gestive heart failure. Of these, 17 had prolonged systemic circulation rates. The earliest roentgenographic changes noted occurred at the lung roots where the outlines of the main trunks of the pulmonary arteries appeared indistinct, and a haze radiating for varying distances into the adjacent parenchyma appeared. In later stages the lung bases, particularly the right, became hazy and a roentgenologic appearance varying from one simulating bronchopneumonia to a pleural effusion appeared. While compensation was being restored the lungs cleared. The hilar engorgement was the last to disappear.

To a certain extent the roentgenographic appearance is reversible. After compensation is restored following the first or second attack the lung fields may assume a normal appearance, and the circulation rates return to normal. After several attacks of failure the hilar congestion becomes permanent and the circulation rate remains prolonged. For this reason it is not uncommon to observe patients who although subjectively confortable still present roentgenographic and circulatory rate evidences of pulmonary congestion. The circulation rates may remain prolonged during the time compensation is being restored. The degree of congestion did not necessarily parallel the degree of retardation of the circulation time, especially in patients who had had previous episodes of heart failure. In this regard it is interesting to note that 11 of the patients in this group had no unusual chest findings on physical examination.

The markings of the lung roots may be obscured by enlargement of the heart. In almost all but the most advanced cases the right lung root can be readily examined. The left hilum is often hidden in patients with advanced right ventricular enlargement or dilatation of the main trunk of the pulmonary artery. Patients in heart

TABLE II

CASES WITH ROENTGEN EVIDENCE OF PULMONARY CONGESTION

Case	Diagnosis (Heart disease)	Valvular Disease	Age	Sex	$MgSO_4$ Time (sec.)	Saccharin Time (sec.)	Ether Time (sec.)	Venous Pressure (mm. H_2O)	Degree of Pulmonary Congestion	Clinical Signs in Lungs	Remarks
1	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	41	M	25.8		10.0	240	+++	Basal râles	
2	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	59	M	33.0		12.0	125	++	o	
3	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	40	F	35.2		12.4	205	++ to +++	o	
4	Hypertensive; arteriosclerotic		74	M	37.8		8.4	212	++	o	
5	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	52	F	26.4		9.7	85	++	o	
6	Rheumatic	Mitral insufficiency and stenosis	25	M	33.0		14.0	130	+++	Basal râles	
7	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	60	F	21.5		7.2	118	+++	Râles left base	
8	Hypertensive; arteriosIcerotic		61	M		23.8	7.0	112	+++	o	
9	Rheumatic	Mitral stenosis	27	F	21.0		6.2	108	++	o	
10	Rheumatic; hypertensive	Mitral stenosis. Aortic insufficiency	42	F		28.0	11.0	185	+	Basal râles	Long standing mitral stenosis
11	Hypertensive		55	M	27.4		8.0	83	+++	Râles right base	
12	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	30	M	28.2		10.2	110	+	o	Long standing mitral stenosis
13	Hypertensive		53	M	17.1		7.0	170	+++	o	Severe anemia
14	Rheumatic	Mitral insufficiency and stenosis	11	M	11.0		4.7	85	+ to ++	o	Rheumatic fever
15	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	59	M	43.0		8.5	125	+++	o	
16	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	13	M	14.9		5.3	120	+	o	Rheumatic fever
17	Hypertensive		49	M	35.0		14.6	55	+++	Râles right base	
18	Hypertensive; arteriosclerotic		69	M	28.0		9.2	50	++	Basal râles	
19	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	38	F		40.0	7.5	150	+++	Basal râles	
20	Rheumatic	Mitral insufficiency and stenosis. Aortic insufficiency and stenosis	31	F		22.0	10.0	230	+++	Basal râles	

failure who have no gross cardiac enlargement, as in certain instances of coronary artery disease, usually show similar changes in both lung roots.

Two of the 3 patients whose circulation rates and roentgenographic findings did not coincide were children with active rheumatic fever and elevated temperatures. The third was an elderly man with hypertension and severe anemia. Both anemia[2] and fever[7,8] are known to accelerate the circulation time even in the presence of heart failure, which explains the apparent discrepancy.

The roentgenographic differential diagnosis between congestive failure and bronchopneumonia is often difficult. Inasmuch as heart failure may be precipitated by an upper respiratory infection or bronchopneumonia, one must keep in mind the possibility of the two processes existing simultaneously. Frequently, however, patients who are well compensated may have bronchopneumonia and retain compensation. In these the roentgenograms may be helpful. If the lung roots remain clear and the main trunks of the pulmonary arteries and their primary subdivisions remain distinct, the probability is that the patient is not in heart failure even though the remainder of the lung fields is mottled. Another differential point sometimes helpful is that bronchopneumonia may be unilateral while congestive failure often involves both lungs. The history, physical and roentgenographic findings and cir-

culation times must all be taken into account when arriving at a diagnosis in obscure cases.

SUMMARY

1. A correlation between prolonged systematic circulation times and roentgenographic changes indicative of pulmonary congestion exists.

2. Fever or anemia may complicate the differential diagnosis by accelerating an otherwise slow circulation rate in the presence of congestive heart failure. In these instances the roentgenographic findings may be of diagnostic importance.

3. Patients who have had previous episodes of heart failure may be comfortable and still present both roentgenographic and circulatory time evidences of congestion.

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THE ROENTGENOLOGIC APPEARANCE OF "BRONCHIOGENIC" CYSTS*

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THE term "bronchiogenic" cyst has been used rather loosely by both roentgenologists and surgeons. True bronchiogenic cysts are probably of congenital origin and may occur either in the mediastinum or possibly within the lung. The majority of cysts occurring within the lung, however, are acquired lesions,[4] and may well represent the end-results of bronchiectasis or lung abscess. The preoperative, differential diagnosis between cyst and lung abscess, encapsulated empyema, neurofibroma, dermoid, lymphoma or malignant tumor is difficult, in some instances impossible. Even an aneurysm or an aberrant goiter may be indistinguishable from a mediastinal cyst.

A study of mediastinal cysts treated at the Massachusetts General Hospital in the past decade was undertaken in order to determine, if possible, any specific roentgenologic characteristics which might be of diagnostic value. Fifteen cases of proved cyst were selected from a larger number in which the diagnosis might be questioned, and are presented briefly. Certain solitary unilocular pulmonary cysts were also studied and 3 cases are described to show their similarity. Multiloculated pulmonary cysts were excluded. The difficulty of diagnosis is shown by the fact that in only 4 of the 15 proved cases was the correct diagnosis suggested in the preoperative roentgenologic report.

Bronchiogenic cysts are usually incidental findings and only occasionally produce symptoms. It seems likely that they will be seen with increasing frequency as mass surveys, like those conducted by the Armed Forces and by the schools, become more widespread.

CASE REPORTS

The cases presented have a fairly similar roentgen appearance. Several, which are not histopathologically typical, are included because of their great similarity to the typical, proved cases. All were operated on —to the extent at least of aspiration—and in those in which the cyst was so located that dissection was impossible the surgeon's note furnished practical, if not histopathologic, proof of the diagnosis. The records have been summarized briefly, indicating

FIG. 1. Case 1. The smooth, ovoid mass lies behind the heart beneath the carina. It appeared to change shape with the different phases of respiration.

* From the Department of Radiology, Massachusetts General Hospital, Boston, Massachusetts. Read before the New England Roentgen Ray Society February 19, 1943.

the reason for admission, the duration of symptoms, and the roentgenographic, operative and pathologic findings.

CASE I. (R. B. U-401331) (Fig. 1). A student, aged eighteen, was studied in his school infirmary for catarrhal jaundice one month before admission to this hospital. Shortly after this, because of a hacking, nonproductive cough, roentgenograms of the chest were made and a chest. After the first attack a dark object, the size of an egg, was noted roentgenoscopically in the right chest. Later, the right chest filled with fluid. This was tapped and guinea pig studies revealed no evidence of tuberculosis. Roentgenologic examination showed the mass in the right posterior portion of the mediastinum behind the base of the heart. It was thought to represent a neurofibroma. At operation a large posterior mediastinal cyst was found, present-

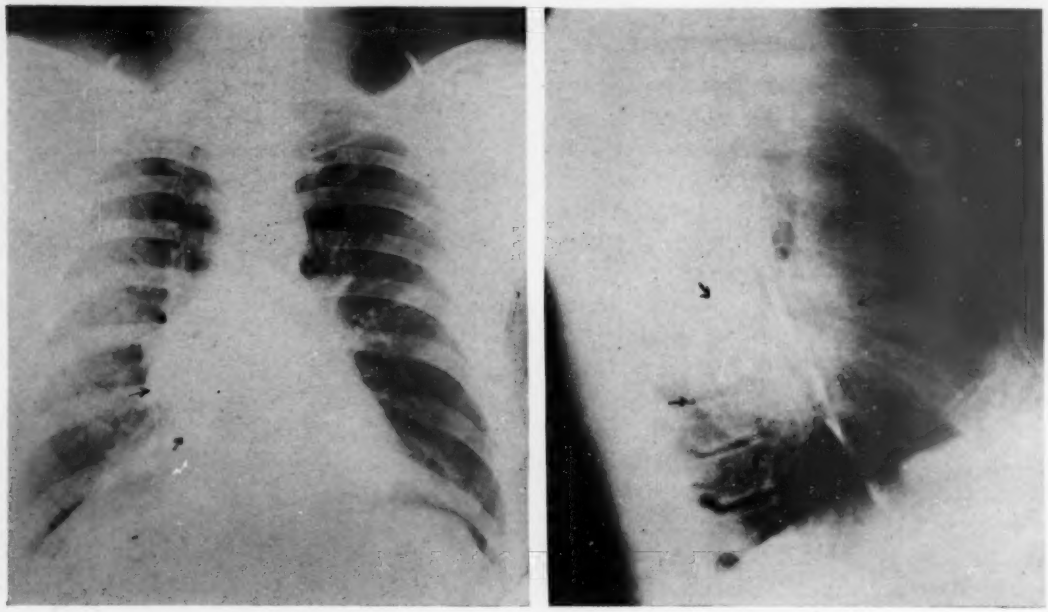

FIG. 2. Case II. Note that the round, smooth mass arises from the posterior mediastinum at the level of the base of the heart. At operation a cyst was removed which showed histopathologically a lining of high columnar epithelium.

mass was demonstrated. He was sent to the hospital for operation. Roentgenologic examination revealed a non-pulsating, ovoid, homogeneous mass 8 by 6 cm. lying beneath the carina. The mass changed shape with respiration.

At operation a cyst was found attached to the right main bronchus. It was removed intact and a histopathologic diagnosis of bronchiogenic cyst was made because of the presence of ciliated respiratory epithelium and cartilage.

CASE II. (H. F. U-85892) (Fig. 2). A twenty-three year old clerk was admitted to the hospital in October, 1937, for diagnosis and treatment. During the six years before entry he had had three episodes of substernal discomfort, with vomiting and severe pain in the right ing against the posterior chambers of the heart. Histopathologically the epithelium of the cyst was of a high columnar type.

CASE III. (E. M. U-354989) (Fig. 3). A thirty-two year old Service man entered the hospital in May, 1942, for treatment of a "lung abscess." He had had intermittent cough, which was productive of occasionally blood streaked phlegm, for one and a half years. Seven weeks before admission he had had "grippe" for one week which was followed by "pneumonia." His cough became worse and was productive of more than two cupfuls of foul smelling sputum each day. The roentgenologic studies revealed a mass which was thought to arise from the superior aspect of the right lower lobe and was diagnosed as a lung abscess. The abscess was

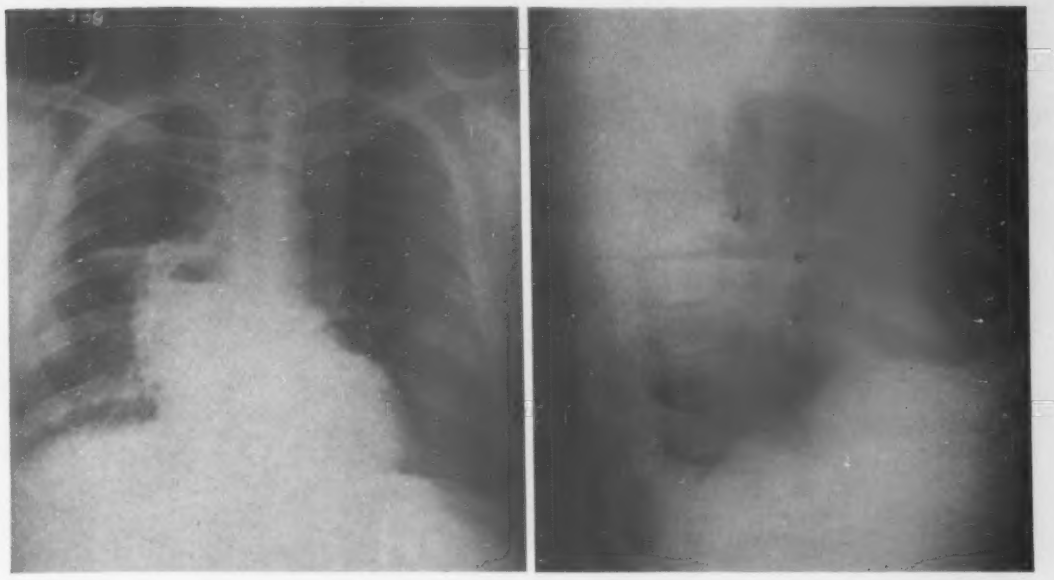

Fig. 3. Case III. A fluid and air-filled cavity is seen in the region of the apex of the right lower lobe. There is relatively little reaction in the adjacent lung, such as would be expected were the lesion a lung abscess of the same duration. At operation a cyst was found arising from the mediastinum.

drained in June, 1942, and in September the patient returned for lobectomy. At this operation a large mediastinal cyst, which was intimately adherent to the right lower lobe, was found. The cyst extended nearly across the mediastinum displacing the esophagus. It was

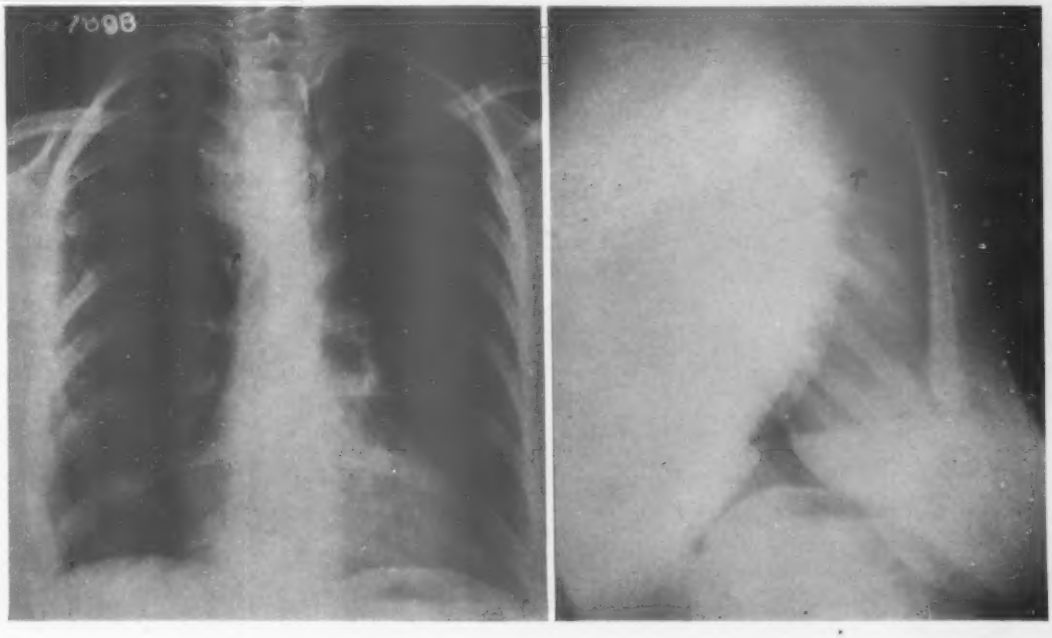

Fig. 4. Case IV. An ovoid mass lies in the right anterior mediastinum displacing the trachea to the left. Roentgenoscopically it was possible to demonstrate that the mass was attached to the trachea and displaced the esophagus but was not connected with it.

free except at the hilum of the lung, and it contained a large amount of foul smelling pus. Histopathologic examination was not made.

CASE IV. (M.S.U-357898*) (Fig. 4). A thirty-six year old housewife was admitted to the hospital in May, 1942, for treatment. Three months before entry she developed rather severe aching, and at times shooting pain, in the left chest above the breast. The pain radiated down the left arm and occasionally to the spine. It was not related to exertion; it lasted from a few minutes to an hour. Two months before admission she was given roentgen therapy of unknown dosage in another hospital and she was symptomatically relieved. In 1932 she had had pneumonia followed by empyema with rib resection.

Roentgen studies revealed a mass in the right upper mediastinum which was attached to the trachea and displaced the esophagus but did not appear to be attached to this organ. At operation a tumor mass was found lying along the right anterior surface of the trachea adherent for approximately 6 to 8 cm. Histopathologic diagnosis was tracheal cyst.

CASE V. (P. S. U-159525†) (Fig. 5). A twenty-five year old housewife entered the hospital complaining of intermittent attacks of vomiting over a period of six months. She had raised a small amount of blood on one occasion. Roentgen examination at this hospital showed a fairly round mass in the posterior mediastinum in front of the eighth dorsal vertebra. The mass measured approximately 3.5 cm. in diameter and lay close to the right border of the esophagus which showed a well rounded pressure defect in this area. The mucosal folds of the esophagus were preserved in the region of the lesion. The mass moved up and down with respiration and upward during the swallowing act. The motion of the mass was similar to that of the esophagus. An intramural, extramucosal tumor was diagnosed. At operation a cyst was removed from the wall of the esophagus. The histopathologic examination showed respiratory ciliated epithelium, smooth muscle and cartilage in the wall of the cyst.

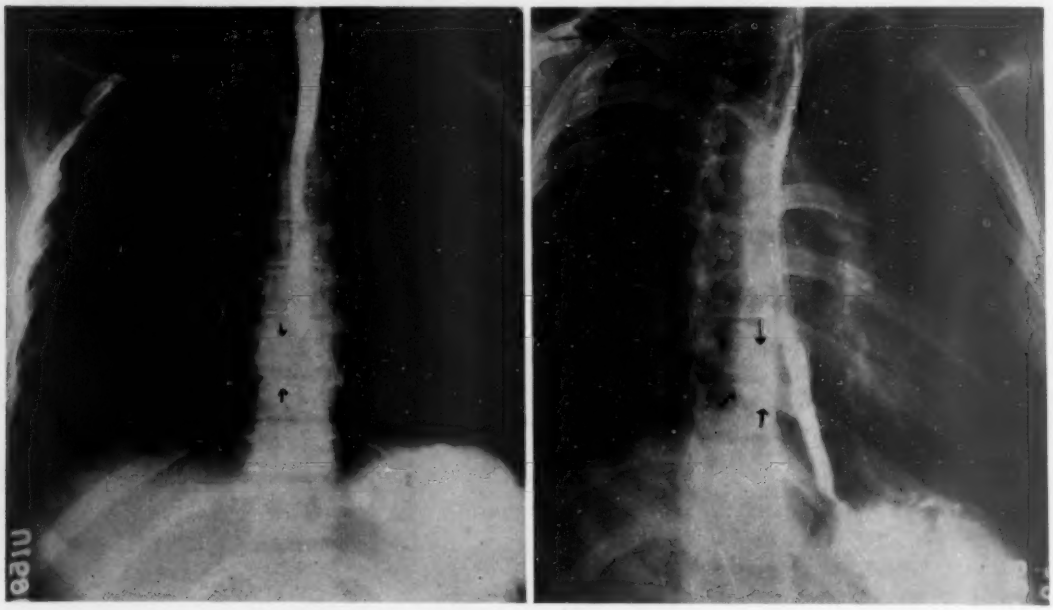

FIG. 5. Case v. A small bronchiogenic cyst was located in the wall of the esophagus and represented an intramural, extramucosal lesion.

CASE VI. (N. M. U-96804) (Fig. 6). A sixty-seven year old housewife was admitted in December, 1937, with complaint of non-radiating epigastric pain of three months' duration. She had no chest symptoms but at the time of

* This case appeared in the Case Records of the Massachusetts General Hospital, Case No. 28412, *New England J. Med.*, 1942, *227*, 560–563.

† This case was reported by Schatzki and Hawes.[5]

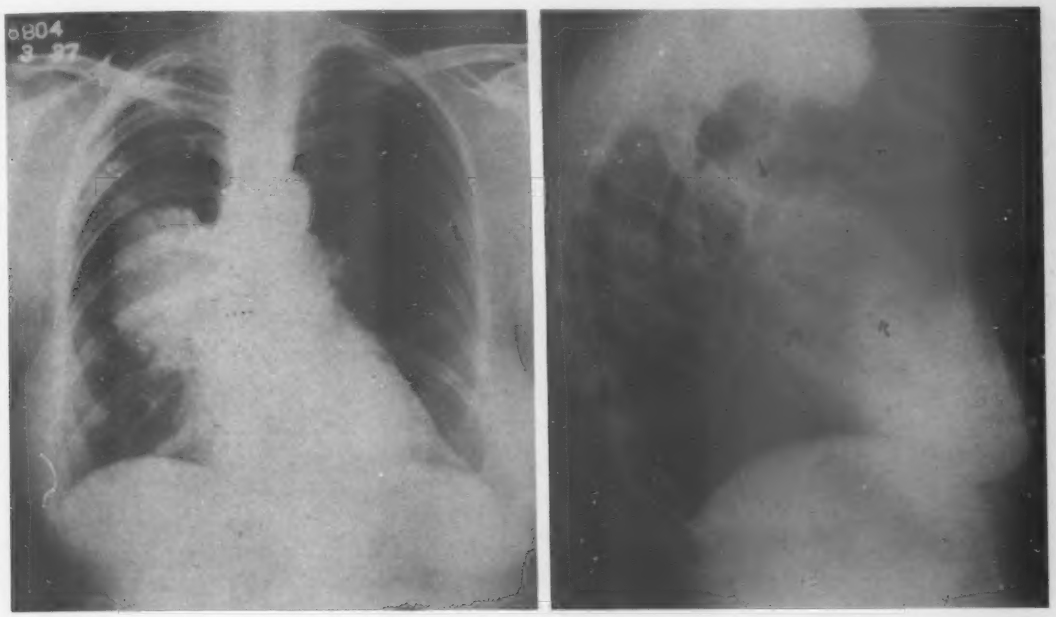

Fig. 6. Case vi. The mass at the level of the right hilum was first thought to represent a tumor arising from a bronchus, but at operation, aspiration yielded thick, mucinous contents, whereby the diagnosis of bronchiogenic cyst was made.

a gastrointestinal examination a mass was discovered in the chest. Roentgen studies revealed a mass in the region of the right lung root which was thought to represent a malignant tumor arising from one of the upper lobe bronchi. At operation a cyst was found which was intimately adherent to the lung and mediastinum. Because of its rich blood supply it was thought inadvisable to remove the mass. It was tapped and yielded thick mucinous material which was characteristic of bronchiogenic cyst.

Comment. It is possible that this cyst originated in the mediastinum but its exact source could not be definitely determined.

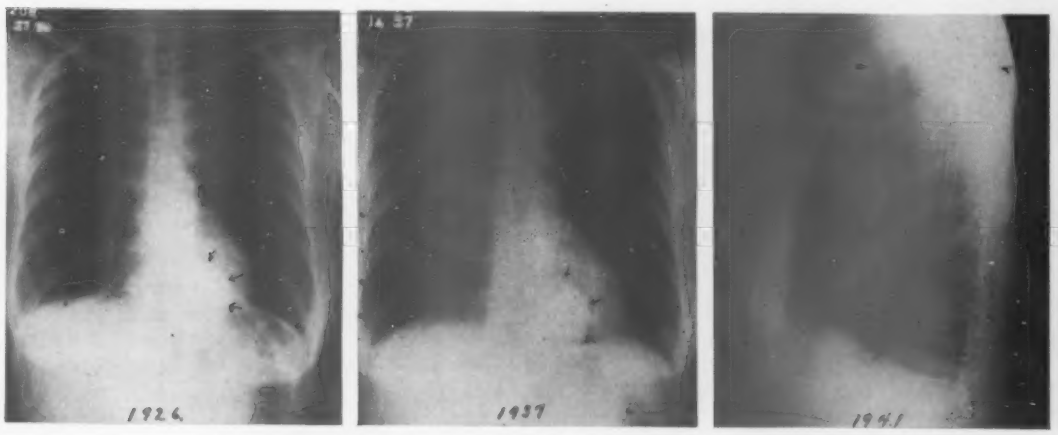

Fig. 7. Case vii. The round mass behind the heart just above the left diaphragm was observed over a period of approximately seventeen years with relatively little change in size. It was removed surgically, and proved to be a bronchiogenic cyst histopathologically.

CASE VII. (A. T. U-55476) (Fig. 7). A sixty-two year old housewife had complained for twenty-five years of pain localized high in the epigastrium with radiation at times to the back. For five weeks before her last admission her symptoms were more severe and almost constant. The mass itself was discovered incidentally at a chest examination in 1926 and since that time had shown very little change. Roentgenograms showed a smooth round mass lying just above the diaphragm in the posterior mediastinum. The mass was not attached to the esophagus. On May 7, 1943, transthoracic removal of the mediastinal cyst and repair of a hiatus hernia were carried out. Histopathologic diagnosis was bronchiogenic cyst because of the presence of ciliated respiratory epithelium and cartilage.

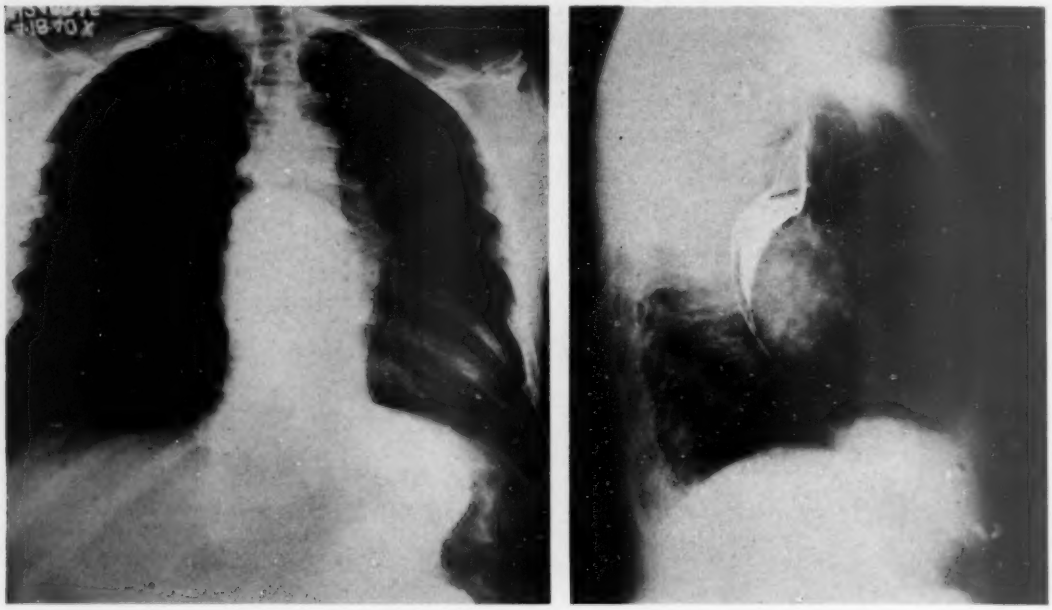

FIG. 8. CASE VIII. The mass lying between the heart and the esophagus was attached to the carina of the trachea by a fibrous cord and involved the wall of the esophagus intimately, but did not invade the mucosa. The histopathologic examination after surgical removal did not show evidence of respiratory epithelium.

CASE VIII. (H.L.U-246015*) (Fig. 8). A forty-two year old clerk was admitted in April, 1940, for study of a mass in his chest which was an incidental finding at a previous roentgenologic examination. He had complained of substernal pain and had had a productive cough for two years. A mass was noted between the heart and the esophagus just below the carina. The mass was attached to the esophagus but did not involve the mucosa. The left lower lobe was collapsed. The mass moved when the patient swallowed; there was no change in its shape with change in the patient's position. At operation a mediastinal cyst which involved the muscular coat of the esophagus was found. The cyst was most adherent to the carina of the trachea. It was thought that a fibrous cord extended from the carina to the cyst and represented the origin of the cyst. Histopathologically there was no epithelial lining and the wall consisted of dense, fibrous tissue in which there were several clusters of lymphoid elements.

Comment. Although the histopathologic findings are not typical of bronchiogenic cyst the location and the cord extending from the carina to the cyst make this the most likely diagnosis.

CASE IX. (O. W. U-56685*) (Fig. 9). A male laborer, aged sixty-three, was admitted in June, 1937, for treatment of a mass in the right anterior mediastinum. He had had a sense of food

* This case appeared in the Case Records of the Massachusetts General Hospital, Case No. 26291, *New England J. Med.*, 1940, *223*, 105–108, and was also reported by Schatzki and Hawes.[5]

* This case appeared in the Case Records of the Massachusetts General Hospital, Case No. 23492, *New England J. Med.*, 1937, *217*, 958–959.

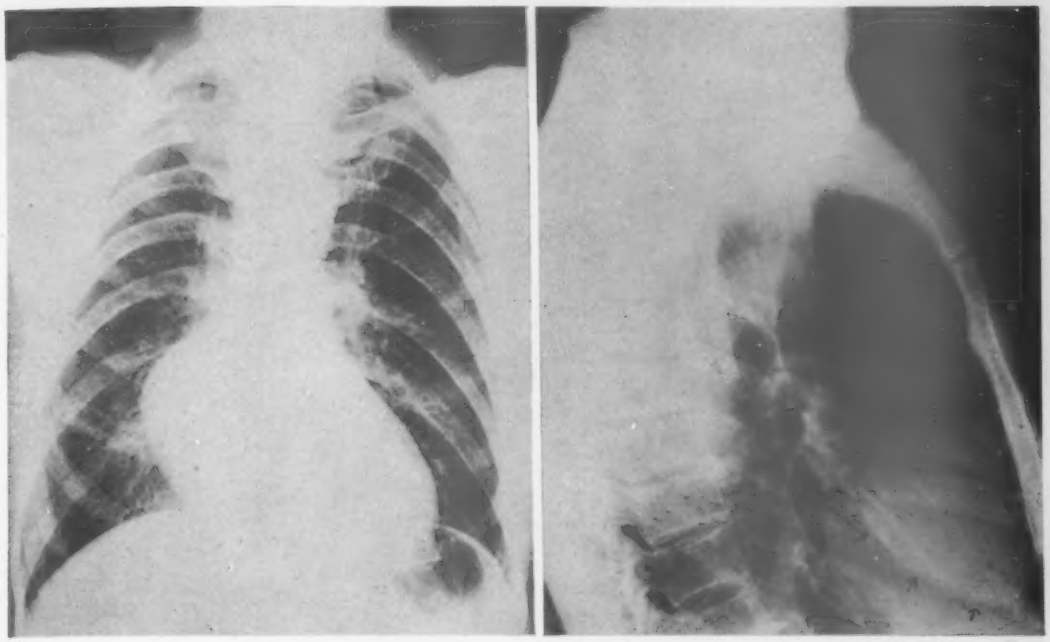

Fig. 9. Case IX. The smooth, round mass arises from the right anterior mediastinum and lies close to the right border of the heart. Histopathologically this proved to be a simple cyst.

sticking in the upper mid-epigastrium without pain, nausea, vomiting or cough over a period of fifteen years. Roentgen studies revealed a mass in the right anterior mediastinum which lay close to the heart and could not be separated from it. It had increased in size over the past six months and was thought to represent a malignant tumor. At operation a large cyst was found lying on the lateral aspect of the mediastinum. This was removed and a second cyst was found above it. The latter cyst could not be removed but was opened and evacuated. Histopathologically it was termed a simple cyst.

Case X. (C.C. U-121816*) (Fig. 10). A thirty-four year old single woman was admitted in April, 1938, for study, because of pain in the chest. She had been well until one month before admission when she developed an upper respiratory infection. Two or three days later she noted a severe, sharp, steady pain in the anterior chest to the right of the sternum. This was aggravated by cough, respiration and motion of the right arm. Roentgenograms taken by another roentgenologist revealed a mediastinal tumor. Roentgenograms at this hospital show a tumor in the right anterior cardiophrenic angle lying against the anterior chest wall and the right border of the heart. At operation a mediastinal cyst was removed. Histopathologically, only a small portion of the cyst showed a persistent epithelial lining of pseudo-stratified cuboidal epithelium. The cyst was multiloculated.

Comment. This case may be of value in linking the other cases of so-called simple or unclassified cysts of the mediastinum into one group, inasmuch as the greater portion of the cyst wall in this case was thin and showed no persistent epithelium.

Case XI. (J. G. U-394942†) (Fig. 11). A thirty year old salesman was referred to the hospital for treatment of a mass in the right upper chest, which had been discovered on a routine roentgenogram. There had been no pulmonary symptoms and none referable to the mass. The chest roentgenograms revealed a sharply defined 8 by 10 cm. mass lying in the posterior aspect of the right upper chest, which roentgenoscopically seemed to move with respiration but not with swallowing. It changed in shape with change in the patient's position. The fourth rib was deformed. The third right interspace pos-

* This case appeared in the Case Records of the Massachusetts General Hospital, Case No. 28422, *New England J. Med.*, 1942, *227*, 606–609.

† This case appeared in the Case Records of the Massachusetts General Hospital, Case No. 29161, *New England J. Med.*, 1943, *228*, 516–518.

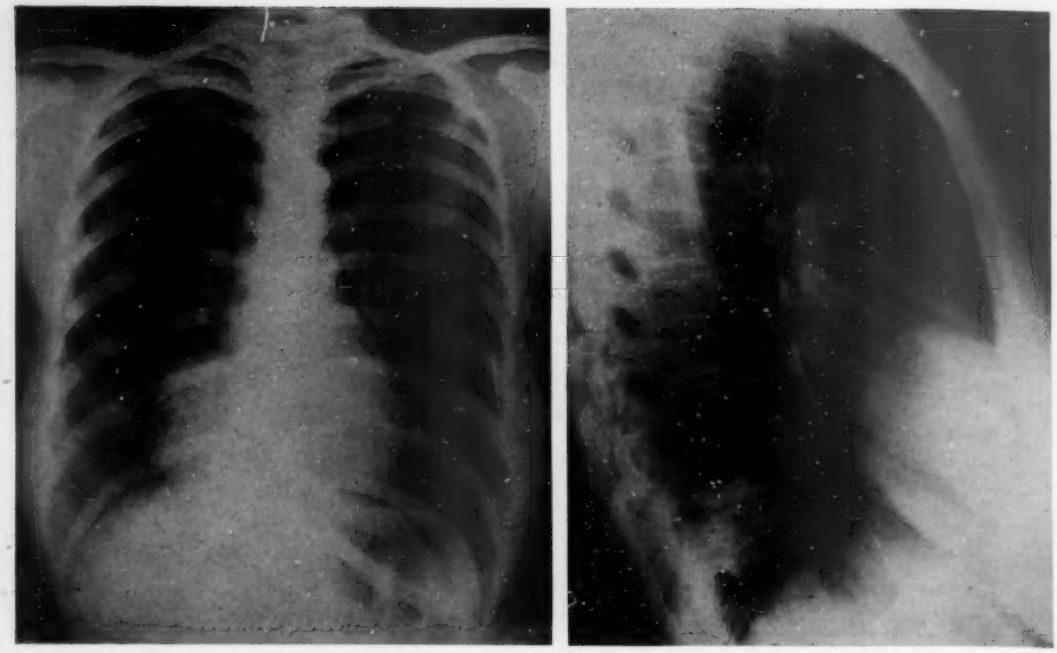

Fig. 10. Case x. The ovoid shadow overlying the right border of the heart was removed surgically. Although most of the cyst wall was thin, a small amount of respiratory epithelium was present in one area.

teriorly appeared to be widened and there was what looked like erosion of the margins of the adjacent ribs. On closer inspection it was decided that the apparent erosion was not actually present, and that the changes could all be explained on the basis of congenital anomaly.

An extrapleural cyst was removed completely. Histopathologic diagnosis was pleural cyst. It was lined with low cuboidal epithelium or mesothelium. The remainder of the wall consisted of a thin layer of connective tissue.

Case xii. (A. S. opd-411932). A housewife, aged forty-two, was referred to the hospital for diagnosis and treatment of a mass in the right upper mediastinum. She had paresthesia, numbness and tingling of the right upper extremity, but no definite chest symptoms. The tumor was discovered three months before entry, and radiation therapy had been given elsewhere without effect. Roentgen studies showed a lobulated tumor of the anterior mediastinum anterior to the aorta. Aspiration was done

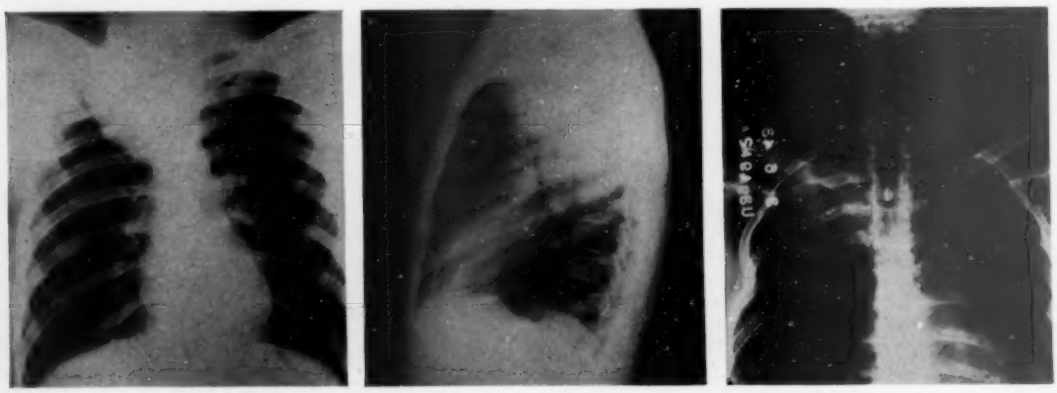

Fig. 11. Case xi. A smooth, round mass arises from the posterior portion of the right superior mediastinum. Congenital anomaly explains the rib changes more logically than does erosion.

through the chest wall and 40 cc. of faintly yellow fluid was removed. Further roentgenograms revealed that the cyst was thin walled. Eight months later the patient felt perfectly well, and the logical diagnosis appeared to be congenital cyst.

Case xiii. (M. C. U-383558) (Fig. 12). A housewife, aged fifty-one, was admitted to the hospital in November, 1942, with the complaint of cough, chest pain, fever as high as

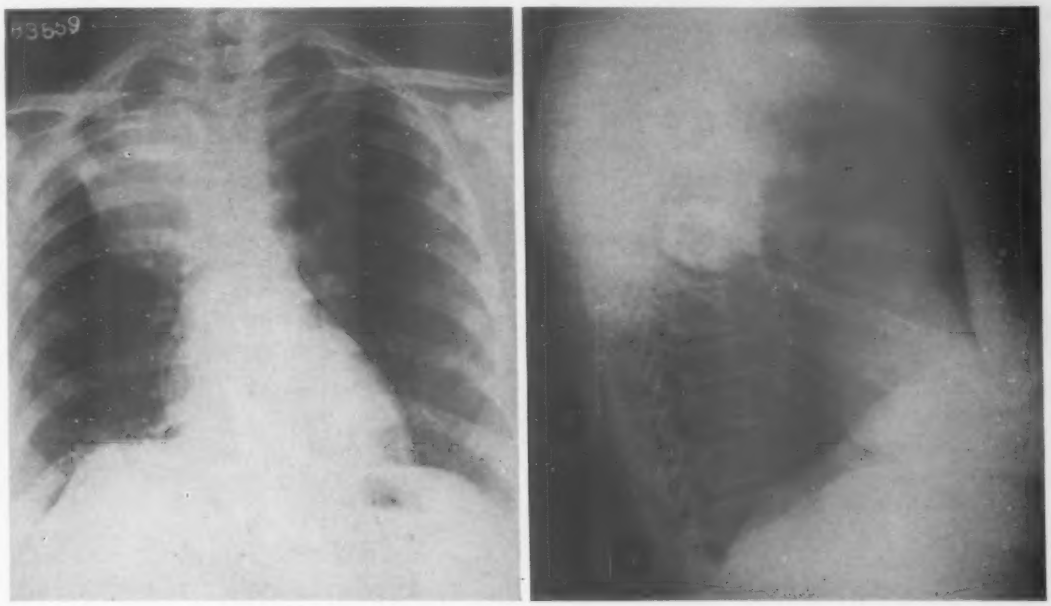

Fig. 12. Case xiii. The relatively smooth, homogeneous mass lying in the posterior portion of the right upper lung field was found at operation to represent a bronchiogenic cyst. It could not be removed, but was biopsied.

104° F., and foul smelling sputum, present for a period of two months. Roentgen studies of the chest revealed a relatively smooth 10 by 8 cm. homogeneous mass arising from the right posterior mediastinum at the level of the third to sixth thoracic vertebrae. The mass pressed upon the esophagus but was not attached to it. A diagnosis of neurofibroma or bronchiogenic cyst was made. At operation an infected bronchiogenic cyst in the right upper lobe was marsupialized. Histopathologic diagnosis was bronchiogenic cyst with chronic inflammation.

Comment. There is some question as to the origin of this cyst. It may have arisen in the right superior mediastinum or in the right upper lobe.

Case xiv. (W. D. U-343755) (Fig. 13). A white male, aged twenty-six, a radio engineer, was admitted for treatment of a cyst of the lung in February, 1942. Four months prior to entry he carried a deer for several miles, and during this exertion he developed dyspnea and pain in the right lower chest. One week later, when he was thought to have pneumonia, roentgen studies revealed pneumothorax, which improved under conservative treatment. Later a diagnosis of cyst of the lung was made and he was referred to this hospital for operation. Roentgenograms revealed a large air-filled cavity occupying the region of the right middle lobe. A diagnosis of pneumatocele was made. A right middle lobectomy was done. The pneumatocele was found to occupy the area of the right middle lobe. A small bronchiogenic cyst which was said to be the size of a hen's egg was found and was interpreted as having acted as a ball-valve mechanism to produce the pneumatocele. The bronchiogenic cyst was not visualized on the roentgenograms.

Case xv. (P. G. U-169510) (Fig. 14). An eighteen year old student was admitted to the hospital in June, 1938, for treatment of a congenital cyst of the right upper lobe. Nine years be-

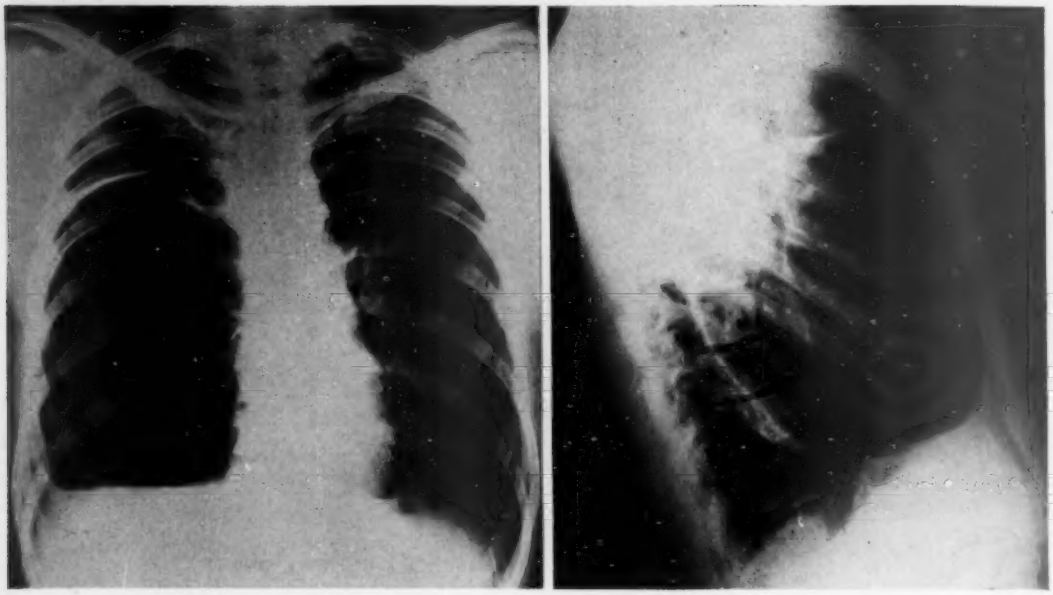

Fig. 13. Case xiv. A large pneumatocele occupies the region of the right middle lobe. At operation a bronchiogenic cyst, not visible on the original roentgenogram, was found and was thought to be the cause of a ball-valve action which produced the pneumatocele.

fore entry, because of a positive tuberculin test, a roentgenogram of the chest was taken, and a lesion in the right upper lobe was discovered, which was eventually diagnosed as congenital cyst. For fourteen months previous to admission the patient had had a rather severe cough which was productive of a small amount of yellow, non-odorous sputum. The roentgen studies at this hospital revealed a thin-walled, fluid-and-air-containing cyst in the lower portion of the right anterior chest. At operation a cyst was removed from the base of the right upper lobe. No histopathologic study of the cyst was made.

Comment. This cyst had previously been diagnosed as a lung abscess because of the fluid and air within the cavity, but the his-

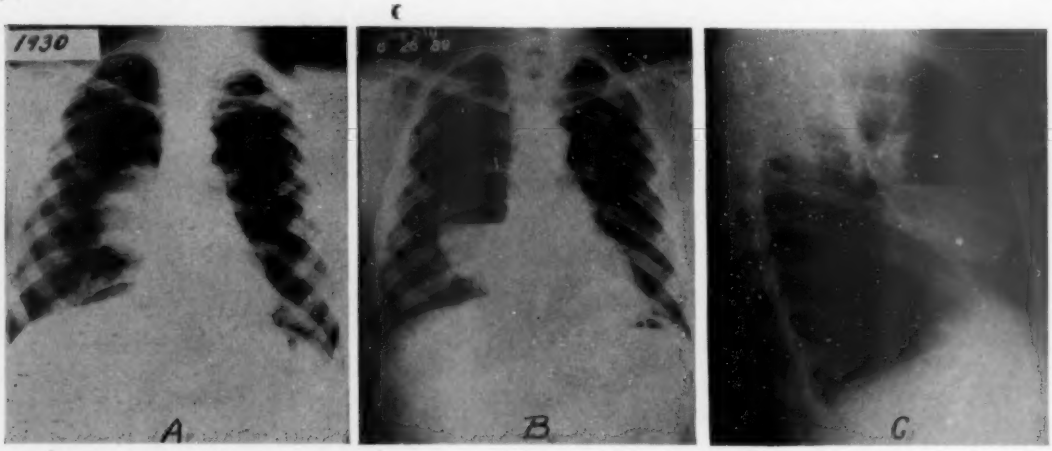

Fig. 14. Case xv. *A*, the mass was demonstrated on a roentgenogram taken because of a positive tuberculin test when the patient was nine years of age. *B* and *C*, roentgenograms taken nine years later. There is a change in the size of the mass. An air- and fluid-filled cavity is visible in the anterior portion of the right middle chest.

tory and previous studies make this diagnosis unlikely. A histopathologic diagnosis was not obtained so that proof of the true nature of the cyst is lacking.

The 3 following cases are probably acquired and not true bronchiogenic cysts. They are included because the question of the diagnosis has been raised and because they are similar to some which have been described in the literature.

Case E. B. (gh-341857) (Fig. 15). A nineteen year old office boy was admitted to the hospital in December, 1934, for treatment of a lung abscess. He had had a chronic cough over a period of three years, which at times was productive of blood. Shortly before the onset of the hemoptysis he had had a tooth extracted, and as a consequence a diagnosis of lung abscess was made, for which he was treated. The roentgen studies were thought to represent tumor or lung abscess. Because of the patient's condition, operation had to be terminated before the lesion was located. He died three days later, and at autopsy an epithelialized cyst was found.

Comment. This case may well represent the end-result of a lung abscess.

Fig. 15. Case E. B. (gh341857). The lesion found in the right upper lobe at autopsy was an epithelialized cyst, but is probably the end-result of an old lung abscess. It has a smooth, round appearance and contains a small amount of air as well as semisolid material.

Case P. G. (U-11534) (Fig. 16). A twelve year old school boy was admitted in June, 1936, for diagnosis and treatment. A tonsillectomy and adenoidectomy had been done six months be-

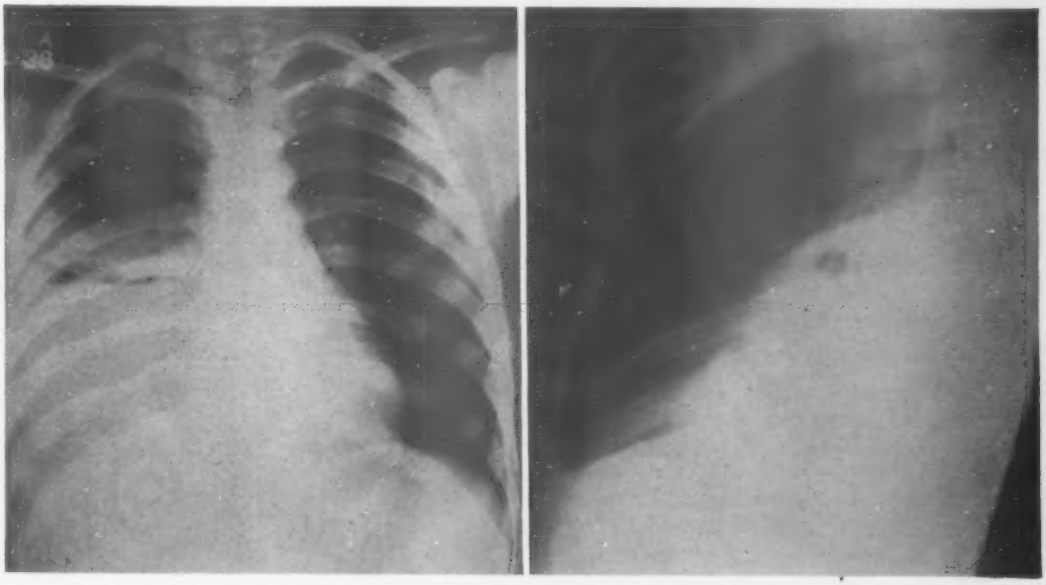

Fig. 16. Case P. G. (U-11534). The large fluid- and air-filled cavity in the posterior portion of the right lower chest could be easily confused with a lung abscess or encapsulated empyema with a bronchial fistula.

fore entry, and this was followed in three weeks by loss of appetite and cough, which at first was unproductive, but later became productive of a large amount of thick, yellow, foul smelling sputum. He also had arachnodactylia and dislocated lenses. The roentgenologic studies revealed dullness in the right lower posterior chest with a fluid level. It was noted at this time that the appearance was not that of a lung abscess although the clinical history was consistent with that diagnosis. After several operations, a right lower lobectomy was done in 1937, and the histopathologic report was "old lung abscess." After further study, however, the diagnosis was revised to "? cyst."

CASE F. K. (U-13924*) (Fig. 17). A housewife, aged twenty-seven, was admitted in November, 1934, for lobectomy. Three years before she had had incision and drainage of what was thought to be a lung abscess. Roentgen studies showed a fluid-and-air-filled cavity in the inferior portion of the left lower lobe in the posterior costophrenic angle. A left lower lobectomy was done, and the histopathologic diagnosis of cyst was made.

* This case was reported by Churchill.[1]

Comment. The last two cases are roentgenologically similar to some of those described in the literature as encapsulated empyema.[2,3] These "cysts" are probably acquired, and not congenital in origin.

DISCUSSION

In a group of 15 bronchiogenic cysts, 8 were in males and 7 in females. Of the latter, the age at onset of symptoms, or at discovery of the lesion, was below forty in 3 and above forty in 4; of the males, it was below forty in 7 and forty-eight years in the eighth.

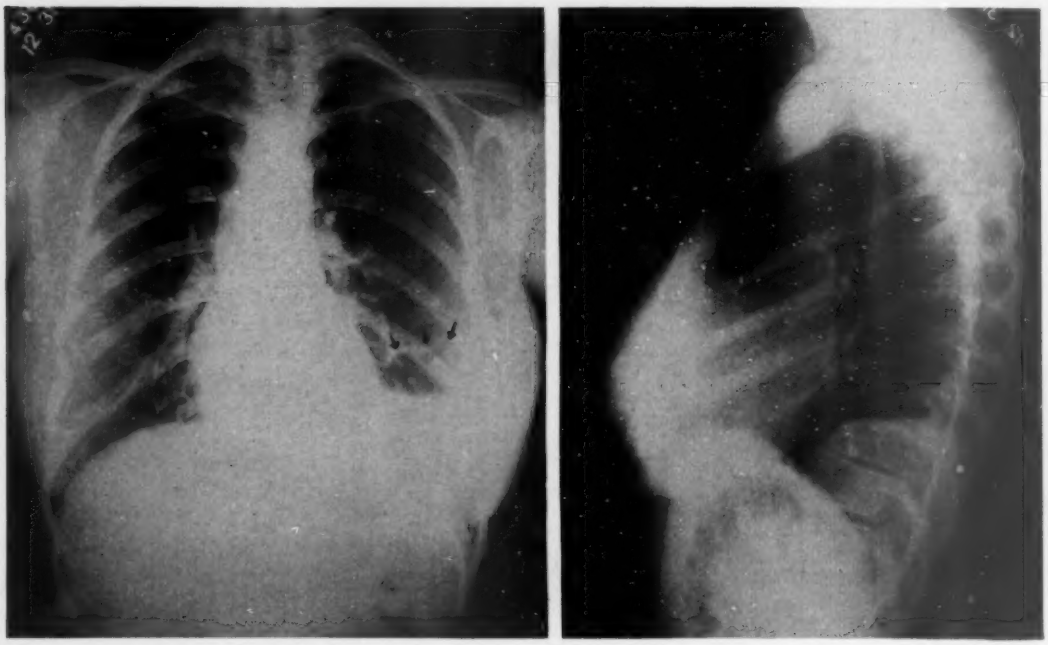

FIG. 17. Case F. K. (U-13924). A fluid- and air-filled cavity is seen in the left posterior costophrenic angle and at operation it was found to represent an epithelialized cyst. This is probably the end-result of an old lung abscess or bronchiectasis.

Unless the cysts become infected their discovery is frequently incidental. Those that are infected simulate lung abscess, or empyema with a bronchial fistula, in symptomatology and somewhat in their roentgen appearance.

The roentgenologic examination should always include roentgenoscopy, which will determine the roentgenograms that should be taken. It will also reveal attachment to

the trachea or esophagus which may not be demonstrated on the roentgenograms. At least posteroanterior and lateral views of the chest are necessary. Roentgenograms taken with the Potter-Bucky diaphragm, as well as barium examination of the esophagus, are definitely important. Laminagrams may be of considerable aid in locating the lesion and demonstrating changes in the adjacent lung tissue or allowing visualization of a cavity not seen in the other roentgenograms.

From the roentgenologic point of view the most important diagnostic characteristic of bronchiogenic cyst is a smooth, round or ovoid shadow arising anywhere within the mediastinum without evidence of bone erosion or calcification. If such a mass is seen lying beneath the carina and there is evidence of tracheal attachment, which is easily demonstrable, this is strong additional corroboration of the diagnosis. (Three cases in the group showed tracheal attachment.) If intramural, extramucosal involvement of the esophagus is demonstrated, as it was in 2 cases, this too adds valuable evidence. It should be remembered that cysts, even if lying within the mediastinum, may show a fluid level, as a bronchus often connects with the cyst. In such cases the roentgenologic appearance of a fluid-and-air-filled cavity suggests a lung abscess, as does the symptomatology of the patient, but there is much less inflammatory reaction in the adjacent lung than is seen in the ordinary abscess. The wall of the cyst may be thin or thick, and the cyst may alternately fill with fluid or drain and contain air. This shift of contents allows definite variation in the size of the shadow seen on the roentgenogram. In 2 of the cases we were able to demonstrate a change in the shape of the mass with change in the position of the patient, and it seems unlikely that this would be possible in a solid tumor. In many instances it is impossible to demonstrate the exact location of the mass, that is, whether it is in the lung or in the mediastinum.

In spite of these findings it may be impossible to make a definite diagnosis from the roentgenographic studies alone. On this account it is particularly necessary to correlate with them the clinical findings. Inasmuch as bronchiogenic cysts are benign it may seem that surgical removal is not justifiable, but because of the difficulty in diagnosis and the technical difficulties after infection has developed, operative interference is generally recommended.

SUMMARY

1. Fifteen cases of "bronchiogenic" cyst are presented to demonstrate (1) their roentgen characteristics, and (2) the difficulty of differential diagnosis.

2. The roentgen diagnosis of "bronchiogenic" cyst is dependent on the finding of (a) a smooth, round or ovoid mass arising from the mediastinum without evidence of bone erosion or calcification within the wall. Additional proof of the diagnosis may be found in the demonstration of tracheal attachment or intramural, extramucosal involvement of the esophagus, if either is present. (b) Those cysts which are infected simulate lung abscess in appearance.

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A DISCUSSION OF THE PATHOLOGY AND HISTOGENESIS OF EWING'S TUMOR OF BONE MARROW*

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EWING'S tumor of bone marrow has remained, ever since 1921, when Ewing first recognized it as an entity, a somewhat elusive and debatable lesion. There are good reasons for this. The cellular composition of the tumor is not fixed and constant as in the majority of neoplasms, but variable and inconstant. The cells composing it are generally undifferentiated but sometimes resemble such widely differing structures as immature red blood cells, reticulum cells, capillary endothelial tubes, and perhaps pseudorosettes similar to those found in neuroblastomas. With such astounding versatility in cellular composition one would expect to find variability in growth activity, and such indeed is the case. There is no set pattern which is always pursued by the tumor so that it can be readily recognized and distinguished from other tumors involving bone; on the contrary, it can be and has been confused with osteomyelitis, with metastases from extraskeletal tumors, especially neuroblastoma, with the osteolytic form of osteogenic sarcoma, with solitary myelomas, and even with angiomas.

There are several reasons why this confusion still exists. In the first place, Ewing's tumor is rare. From 1906 to date the Surgical Pathology Laboratory of Columbia University has been able to collect only 42 cases; 26 from the Presbyterian and Babies Hospitals and the rest from other sources. Eight other cases which simulated Ewing's tumor have been excluded. Two were osteolytic osteogenic sarcomas, 2 were possibly metastases from neuroblastomas, 2 were metastases from carcinomas, and 2 were myelomas, one plasma cell and the other myelocytic.

Of the 42 accepted Ewing's tumor cases only 14 were treated by radical resection and only 2 were autopsied; so that very little material in bulk was available for study. Add to this the facts that natural or irradiation-induced necrosis often ruined the material, and that much of it received unsatisfactory histological preparation and it will easily be appreciated that the harvest of thirty-five years is lamentably meager and has made adequate study impossible. When we turn elsewhere for larger groups, the same unsatisfactory conditions exist. Crowell reported in 1935 that there were only 109 cases in the Registry of Bone Sarcoma. These had previously been studied in part by Kolodny (1927) and Connor (1926, 1934) and they include some of the cases composing other large groups such as those of Coley (1935) who studied 115 patients from the Memorial Hospital, and some of the 135 cases from Johns Hopkins Hospital reported by Geschickter and Maseritz (1939). Other large groups are the 114 cases from the Mayo Clinic summarized by Meyerding and Pollock (1940) and Meyerding and Valls (1941) and 30 patients examined by Campbell and Hamilton (1941). From such groups we may learn something about site of origin, rate of growth, spread and metastasis, but nothing but speculations about histogenesis and much confusion about histopathology. For clarification of the latter we must seek further afield.

Certain features of the tumor are well established and the present group of cases tends to confirm them. Ewing's tumor is a growth more common in males (60 per cent) than in females (40 per cent). It is found especially in childhood and youth (63.2

* From the Laboratory of Surgical Pathology, College of Physicians and Surgeons, Columbia University, and the Department of Surgery, Presbyterian Hospital, New York. Presented by Dr. Ross Golden at the Forty-third Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 15–18, 1942.

per cent of the Columbia University patients were less than thirty years old), but the age variation extends from four to seventy-nine years so that no age can be regarded as exempt. The growth of the tumor is generally rapid; in 79 per cent of this group of patients the known duration of symptoms was less than a year. Pain was a feature of the growth of 80 per cent and this was sometimes accompanied by fever and even leukocytosis. Although commencing within the bone, it spreads rapidly to the tissues outside of it. This had occurred in all of the 41 of these cases in which such information was available and frequently the extra-osseous growth made an easily palpable mass which was much greater than the intra-osseous involvement.

The distribution according to bone of origin in this group is shown in Table 1.

This group has a disproportionately large number of cases in the bones of the head, probably because of a large department of dental and oral surgery connected with our institution. Otherwise it conforms with the experience of others.

The site of origin within the bone is generally conceded to be from the soft tissues rather than from the osteoblasts of the bony framework. Ewing (1921, 1924) originally described the tumor as affecting the shafts of the bones and not their ends, and he was impressed by the extensive involvement of the shaft. He found that the tumors permeated through the periosteum and widened the shaft, and he recorded the large size of the growth in the soft parts. Some later students, because they observed cases in which the bony involvement seemed limited to the haversian canals and the subperiosteal layer, have suggested that all Ewing tumors start in these places and never in the medullary canal. The chief exponents of this conception have been De Santo (1934) and the late W. B. Coley (1935). It seems to me impossible either to confirm or deny this contention since the majority of cases show extensive involvement of the medullary canal as well as the haversian and subperiosteal regions. So far as present information goes, one can only say that apparently the tumor may start anywhere in the soft parts of the bone, although it is probably very rare in the epiphyses.

Table I

DISTRIBUTION OF 42 CASES OF EWING'S TUMOR OF BONE RECORDED IN THE SURGICAL PATHOLOGY LABORATORY, COLUMBIA UNIVERSITY 1906–1942

Lower extremity	11	(Femur 5, tibia 4, fibula 2)
Head	9	(Maxilla 4, mandible 3, skull 2)
Upper extremity	7	(Humerus 6, radius 1)
Thoracic cage	6	(Rib 5, sternum 1)
Pelvic girdle	4	(Ilium 3, pubis 1)
Shoulder girdle	3	(Scapula 2, clavicle 1)
Vertebrae	2	

Fig. 1. P. P., male, aged fourteen. Ewing's tumor of lower end of radius of six months' duration with enormous periosseous involvement.

Almost all writers agree with our own experience that the tumor itself does not form bone or cartilage. Neely and Rogers (1940) believe that even this may be possible but they do not offer any proof of it. Most authors stress the fact that, with the infiltration of the haversian system, destruction of preëxisting bone and weakening of the bony structure, new bone may be laid down in layers paralleling the long oxis and producing an onion skin effect. In aur experience this may occur but is is uncommon. Certainly, it is not pathogno-

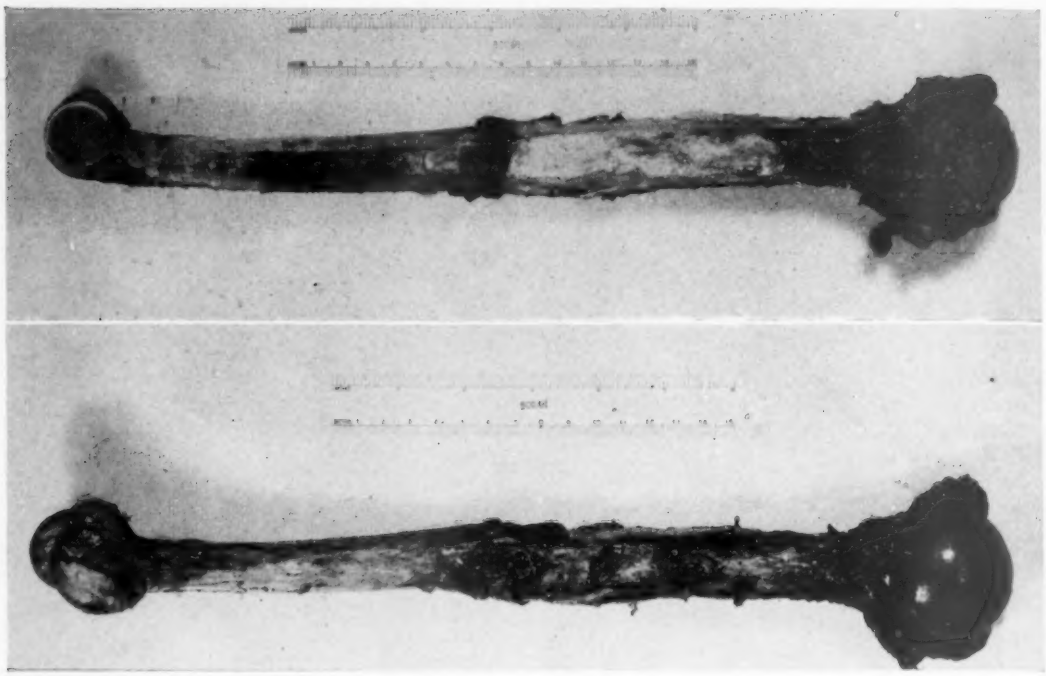

FIG. 2. L. C., male, aged seventy-six. Ewing's tumor of upper two-thirds of shaft of humerus with widening of the marrow cavity and shaft, and complete necrosis of all tumor tissue following irradiation. Four months' duration.

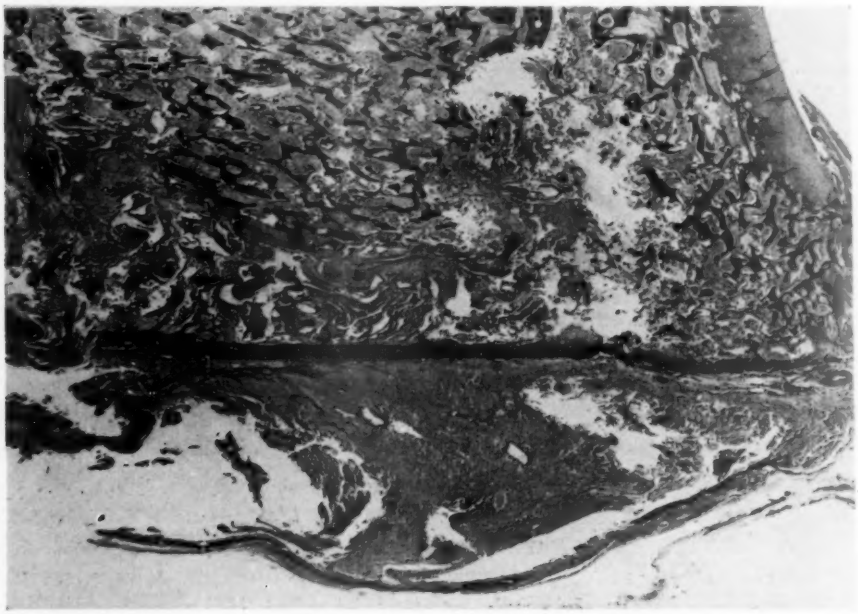

FIG. 3. Photomicrograph from the case illustrated in Figure 1. The lower end of the radius with extensive infiltration of the cancellous bone, penetration of the cortex, and extensive elevation of the periosteum by the tumor.

monic of Ewing's tumor nor does it occur exclusively in that disease. More frequently when the bone is weakened by the destructive process, new bone is formed in the region of the periosteum without any very definite pattern. Very commonly the destructive growth widens the shaft and tends to produce a honeycomb effect in the remaining bone.

Grossly the tumor tissue tends to be soft and has a pallid appearance which may be affected as to color by necrosis and hemorrhage. Necrosis is common both as a phenomenon of rapid growth and also as a post-irradiation effect (Fig. 2). The tumor spreads by infiltrative growth both inside of the bone and in the surrounding soft parts (Fig. 1 and 3). Metastasis is common and takes place chiefly through the blood stream. The commonest sites for the lodgment of metastases in our experience have been the lungs and bones. One can never feel sure when considering subsequent involvement of other bones whether it is a phenomenon of metastasis or multiple primary tumors. It has not been common in autopsies to find metastases widespread in other organs and tissues.

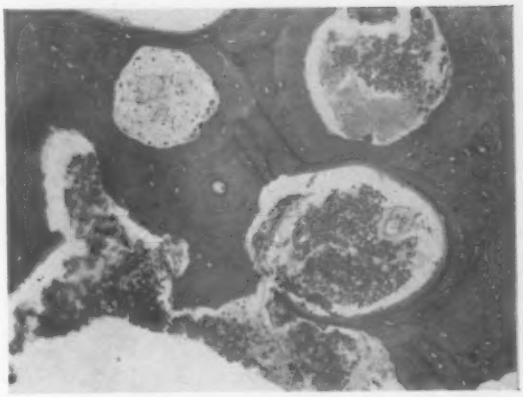

Fig. 4. T. M., female, aged seventeen. Ewing's tumor of the femur invading the haversian canals of the cortex.

The histopathological picture is difficult to record because in my experience, it is the most complex and poorest defined in all oncology. After attentive study of the material at my disposal, I lack a clear and definitive mental picture, which on the basis of histopathology alone, enables me

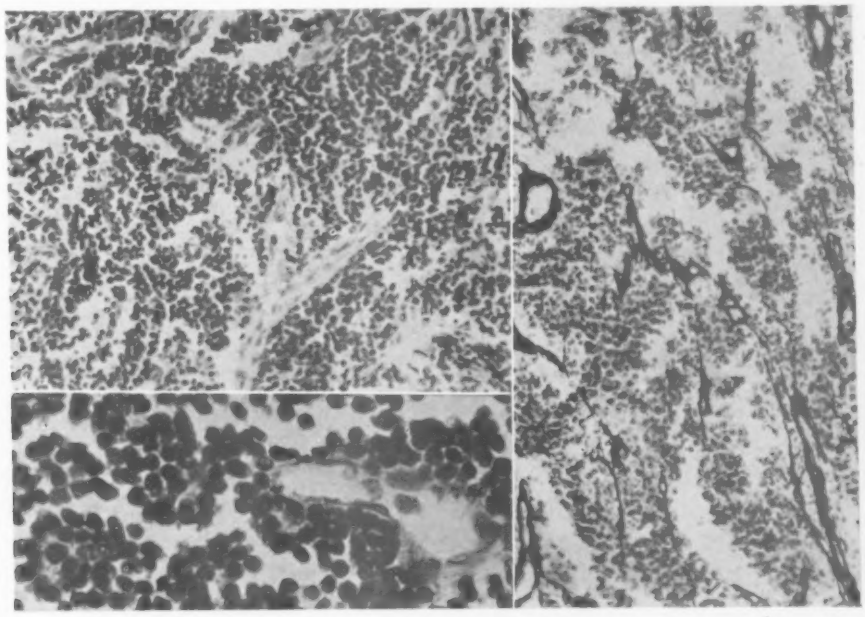

Fig. 5. E.R., female, aged forty-four. Ewing's tumor of the tibia. Composite picture showing characteristic histopathological morphology. Small, undifferentiated cells arranged in cords without reticulin formation and with fibrous bands separating the cords. Hematoxylin and eosin and Laidlaw stains. ×245 and ×635.

to differentiate this neoplasm from others involving bone which closely resemble it.

The basic make-up of the tumor consists of solid cords of cells. These are separated by bands of fibrous tissue varying from thick to thin. Sometimes silver will bring out delicate reticulin fibers between the individual cells and sometimes these are absent. The cells themselves are generally rounded but close packing may mold them into a polygonal shape. The size of the cells is variable, usually from two to four or even more times the size of a small lymphocyte. In the Columbia University material, if smaller cells are present it has always been due to degeneration which is of frequent occurrence. The nuclei commonly are rounded and the cell outline usually is indistinct (Fig. 5). A not infrequent variation of this basic picture is the presence of capillary blood vessels. These may be found in the centers of the collagenous septa, or in more intimate relationship with the tumor cells, the red blood cells being separated from the tumor cells only by endothelium and delicate strands of reticulin (Fig. 6). Occasionally, according to Oberling and Raileanu (1932), vascular channels are formed whose walls are composed of endothelioblasts, heaped up and projecting into the lumen. This last formation was not recognized in any of my material.

A good many authors believe that reticulum cells are present in some tumors. These are to be recognized by the larger size of the cells, by the kidney shape of some of the nuclei and by the presence of reticulin fibers among some of the tumor cells (Fig. 7). Oberling (1928, 1932, 1942) insists upon this and many agree with him. On the other hand, Ewing (1942), Parker and Jackson (1939), Simmons (1939), Szutu and Hsieh (1942), Edwards (1940) and others, are quite certain that primary reticulum cell sarcoma of the bone marrow is a different tumor and that there are no reticulum cells in Ewing's tumor. Foot (1942) and Warren (1942) are inclined to agree with this viewpoint. I must confess

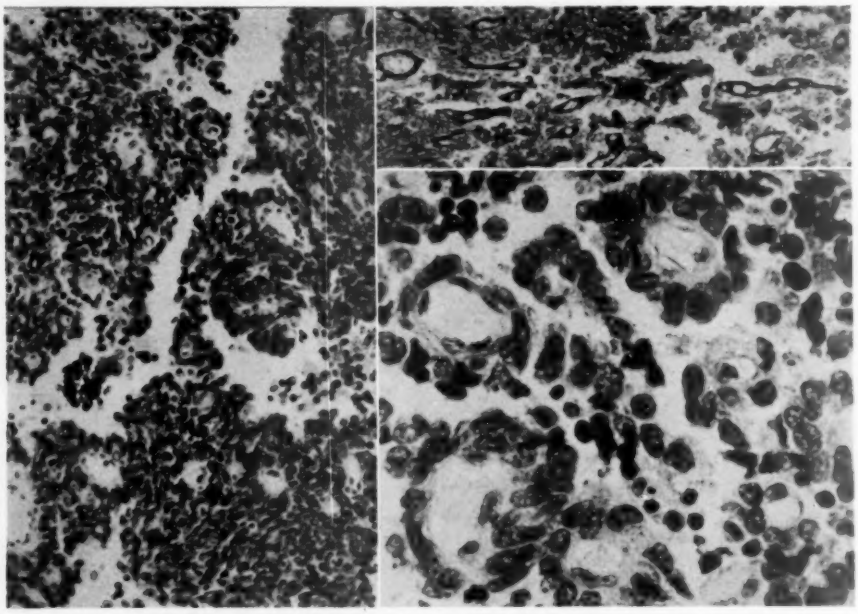

FIG. 6. G. G., female, aged thirty-three. Ewing's tumor of rib. Composite picture showing undifferentiated cells with special orientation about the many capillary blood vessels. No reticulin formation. Hematoxylin and eosin and Laidlaw stains. ×245 and ×635.

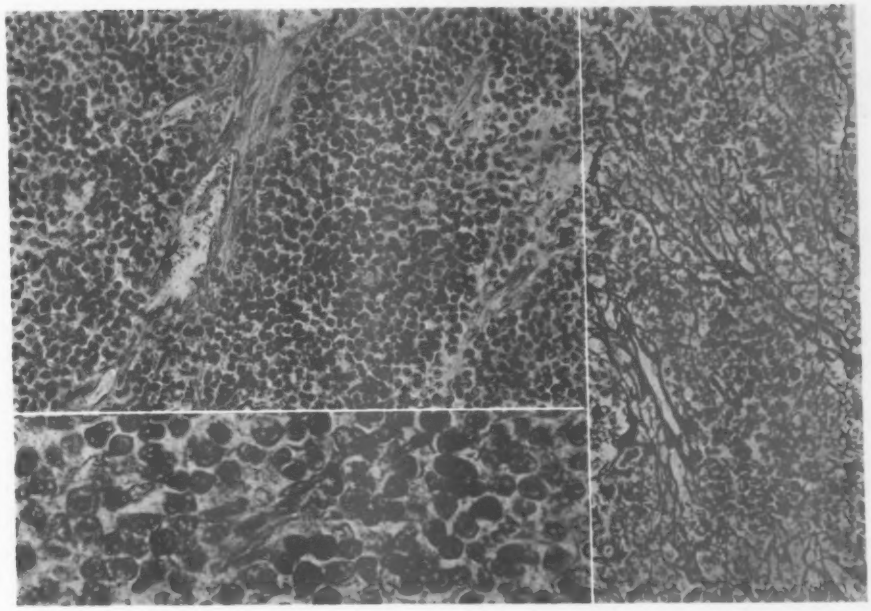

Fig. 7. E. DeV., male, aged nineteen. Ewing's tumor of rib. Composite picture showing the characteristic arrangement of cell cords and fibrous septa but with cells of the reticulum type which have reticulin fibers between them. Hematoxylin and eosin and Laidlaw stains. ×245 and ×635.

that after studying my own material, I feel unable to separate reticulum cell sarcoma and Ewing's tumor into two groups. The two seem so intermingled so far as their cellular composition is concerned that I must agree with Oberling that they are simply variants of the same tumor.

The next feature which appears in some of the tumors is the presence of pseudorosettes (Fig. 8). These are definitely rounded structures made up of columnar cells arranged in a ball with their nuclei all oriented at the outer or circumferential poles and the naked cytoplasm projecting toward the central point of the ball. It is common knowledge that such structures form one stage in the development of the sympathetic nervous system and that they not infrequently appear in neuroblastomas (sympathicoblastomas). If properly fixed and impregnated with silver, it will usually be found that neurites project from the central pole of the cells forming the pseudorosette. The presence of these pseudorosettes in some tumors in bone and the fact of not infrequent multiple bone involvement has led Colville and Willis (1935), Willis (1940), and Sternberg (1935) to express the belief that all Ewing's tumors are really metastases from occult primary neuroblastomas which, as is well known, frequently metastasize to bone while the primary tumor remains small and occult. No doubt some cases called Ewing's tumor

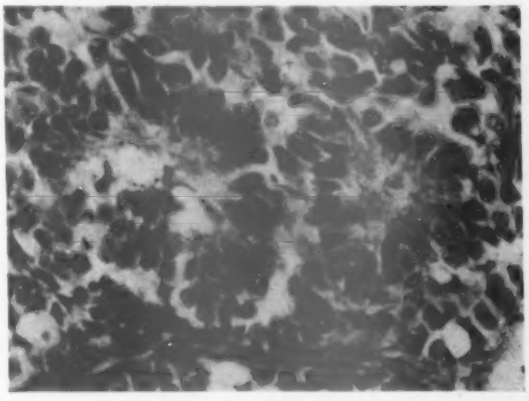

Fig. 8. E. S., female, aged eleven. A tumor which has formed pseudorosettes, one of which shows central vacuolation. Ewing's tumor or sympathicoblastoma? ×780.

are really metastases from neuroblastomas as Willis contends. Connor (1934) acknowledged in his second paper that some of the cases recorded in his first paper (1926) were probably metastases. But this will not explain Gharpure's (1941) case which had many pseudorosettes and yet at autopsy showed tumor tissue only in the femur and the lung, nor the case of Gratz (1930) which was autopsied and had no area involved which might have been a primary neuroblastoma. Moreover, the reported cures of over five years, including the one in our series who has now lived thirty-two and a half years, can hardly be considered as cures of neuroblastomas with metastases. No one, so far as I am aware, has demonstrated neurites connected with the cells of the pseudorosettes in primary bone tumors. But if they are not composed of neuroblasts, what can they be? Gratz (1930) suggested that they were imperfectly formed capillary blood vessels, but to me this seems incredible. No observations in embryology nor on tissue cultures and no reports of the histopathology of blood vessel tumors have ever described comparable formations. Oberling (1942) does not allow himself to be puzzled by these structures which he does not believe have any histogenetic significance. He thinks the formation of the pseudorosette is due to degeneration and necrosis with the radiating disposition of the surrounding cells to be explained on a purely physical basis. He says that he has seen them in various tumors, especially small cell mediastino-pulmonary tumors which he is sure are not sympathicoblastomas (neuroblastomas). I must confess that this explanation does not fully satisfy me. Orientation of the nuclei toward the peripheral pole has a teleological aspect which suggests an activity other than pure degeneration. Consequently, their presence in true Ewing's tumors remains for me unexplained and in need of further elucidation.

This extraordinary tumor apparently does not end its activities here. Although I cannot confirm the observations from my own material, the formation of still other cell types has been reported on rare occasions. Oberling (1928), Oberling and Raileanu (1932) and Roome and Delaney (1932) have found in some tumors embryonal types of red blood cells and a variety of white blood cell types, including myelocytes and finally plasma cells and macrophages.

This brings us finally to a discussion of the cellular origin of Ewing's tumor. It is quite apparent that this must be hypothetical and it will vary depending upon the number and variety of cell types which the architect of the hypothesis is willing to admit can properly be included. Ewing (1942) still adheres to his original conception that the tumor is derived "from vascular endothelium with angioblastic properties" and he cites the case of Foote and Anderson (1941) as properly illustrative of the three different kinds of tissue which can be formed, i.e., solid masses of undifferentiated cells, vascular tubes surrounded by cells and rosettes (pseudorosettes?). Cases in which there are reticulum cells, myelocytes, plasma cells, red blood cells and hemohistioblasts he refuses to accept. Further, he says: "I know nothing about any relation of embryonal cells to this tumor." If I understand Ewing correctly, he means to include in the term vascular endothelium certain undifferentiated adventitial cells. The exact nature of these cells is not clear to me.

Oberling's conception of the cellular origin of the tumor differs from this. At my request he recently restated his position as follows: "I have no doubt that Ewing's tumor is a reticulosarcoma, that is to say, a tumor derived from the young reticular cell (cellule réticulaire jeune), which most frequently is seen as a cellular blastema without any differentiation. But in certain cases differentiated cell forms appear and then one may see adult reticular tissue with abundant production of argentophile fibers, cells with an endothelial aspect and myeloid forms. . . . These differentiations can only be explained if

one considers as stem cell the young reticular cell of the hemopoietic organs; in other words, something like the hemohistioblast of Ferrata." Continuing his discussion he writes: "This hypothesis besides is in harmony with the fact that tumors identically like reticulosarcoma of the bone marrow can be found in all organs which have a reticular stroma, notably the lymph nodes, the spleen and the liver. I had in my collection lymph node tumors and a splenic sarcoma which every observer not previously warned would have accepted as Ewing sarcomas. . . . The myelomas are near relatives of the reticulosarcomas in the sense that the latter can produce in exceptional cases pictures very closely resembling myeloma. Nevertheless, the myeloma keeps its own individuality and hence must be separated from Ewing's sarcoma just as the lymphosarcoma (lymphocytic and lymphoblastic) must be separated from lymph node reticulosarcomas." Oberling tries to reconcile his hypothesis with that of Ewing in the following manner: "Moreover I believe that what separates my hypothesis from that of Ewing on the histogenesis of these tumors is a question of nomenclature rather than any fundamental difference. When Ewing says in his treatise (4th edition, p. 368), 'These observations suggest that the process begins in the perivascular endothelium,' I believe that he intends to designate by that term the perivascular cells with endothelial potentialities. Now these cells, from all the evidence at hand, are young reticular cells." But Ewing will have none of this. For him the stem cell of the tumor cannot form reticulum cells nor red and white blood cells. If any of these cells are formed, then for him the tumor is either a reticulum cell sarcoma or a myeloma.

It does not seem to me fruitful at the present time to pursue further a discussion of the histogenesis of Ewing's tumor. Variants of these two hypotheses have been published but not by men with the ripe experience and broad histopathological training of Ewing and Oberling, and they do not express any important variations. In addition to these two, I asked three other men whose opinions in oncology when expressed demand respectful attention, for their ideas about the histogenesis of Ewing's tumor. They were N. Chandler Foot, Pierre Masson and Shields Warren. In effect their answers were all the same: they did not know. This, too, is my own position. I am inclined to favor Oberling's hypothesis rather than Ewing's for several reasons: I believe from a study of my own material that reticulum cells often form part of the tumor; Oberling's embryological background seems to me to be on a sounder basis than Ewing's; and finally, I have never understood exactly what Ewing means by vascular or perivascular endothelium. But before the histogenesis of the tumor can be settled, more experimental work will have to be done. It is to be hoped that some Ewing's tumor tissue can be obtained in a viable sterile status for explantation *in vitro*. I believe that the histogenesis of many debatable tumors can be elucidated by the method of tissue culture, and I hope that the opportunity may arise for such studies to be carried out by Dr. Margaret Murray, whose experience in this work is unique. If this occurs and new facts are learned, it may be possible to clear up the enigma of Ewing's tumor. Without more facts, I feel that this problem belongs, as Foot (1942) has so aptly said, in the docket of unfinished business.

SUMMARY

The principal features of the pathology of Ewing's tumor of bone marrow have been set forth and the hypotheses of Ewing that the tumor is derived from vascular or perivascular endothelium and of Oberling that it is derived from young reticular cells have been discussed. Although I favor the latter hypothesis I believe that no conclusions regarding histogenesis are possible with our present knowledge.*

* For discussion see page 353.

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THE ROENTGENOLOGIC ASPECTS OF EWING'S TUMOR OF BONE MARROW*

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INTRODUCTION

EWING first recognized in 1921[4,5] the tumor which bears his name. He described it as an endothelial myeloma, a tumor arising in bone marrow, and considered its origin to be from vascular endothelium. Since that time there has been much controversy regarding its histogenesis and pathologic classification. While the literature is not lacking in discussions relative to the protean aspects of this disease entity, if such it be, it seems justifiable to present a review of another group of cases because of the continued interest in the controversial points regarding the tumor's cellular origin as well as its clinical course. The roentgen features will be stressed particularly since in our experience they are as variable as the histopathologic structure.

Twenty-six cases of Ewing's tumor have been collected from the files of the Presbyterian Hospital and the Medical and Surgical Pathology Departments of Columbia University College of Physicians and Surgeons (1906–1942). All are proved histologically and have fairly complete clinical and laboratory data available with approximately 88 per cent follow-up. An additional 16 cases are available for study from a pathologic standpoint only.

Elsewhere in this issue of the JOURNAL, the pathology and histogenesis of this tumor is discussed by Dr. Arthur Purdy Stout. It would, therefore, be superfluous to discuss any part of this problem other than to emphasize again that the histogenesis of Ewing's tumor is still disputed. Its cellular composition varies and because of this there are those who consider it a variant of reticulum sarcoma rather than a tumor "from vascular endothelium." The varying cellular composition is as variable as its clinical and roentgen manifestations and rate of growth.

The youngest patient in our series was four years of age and 2 others were in the first decade of life. The oldest patient was seventy-nine years of age, with one other in the eighth decade. The majority of cases fell in the period between ten and thirty years, with 10 in the second decade, 5 in the third, and 3 each in the fourth and fifth. The average age was twenty-four. Eleven were female and 15 male. Localized pain was the important initial clinical manifestation in all but a few. In the others, an abnormal swelling was the first evidence of disease. Trauma might have played a part in about a third of the cases. Intermittent fever and leukocytosis were often present.

Apparently no portion of the skeleton is immune but the initial lesions in our series occurred most frequently in the humerus, ribs, femur, and ilium, in that order. One tumor occurred in the temporal bone. Extra-osseous involvement was almost an invariable finding. Eventually involvement of other portions of the skeleton was common and perhaps occurred more often than we have evidence of since not in all cases was a complete examination of the skeleton done. A metastasis to the lungs is a common terminal episode; also to the brain and other viscera.

The time elapsing between the onset of symptoms and the clinical examination was usually a matter of months, the shortest being one month, the longest forty-eight, and the average eight plus months. Only 2 patients in our series are known to be alive and well long enough to consider them probably permanently ar-

* From the Department of Radiology of the Presbyterian Hospital and of the College of Physicians and Surgeons of Columbia University. Presented by Dr. Ross Golden at the Forty-third Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 15–18, 1942.

rested. The first is a unique case recently reported in the literature by B. C. Smith[9] as a thirty-two and one-half year follow-up, after amputation of the involved femur. The second is one treated by irradiation alone, involving the spine; alive and well after six years. Three cases are too recent to evaluate. The average duration of life in the others, regardless of the method of treatment employed, was fifteen months; the shortest two months, and the longest seventy-five months. This last case was one in which the humerus was involved. The patient was treated with extensive irradiation only to succumb in the seventh year from pulmonary metastasis.

ROENTGEN FINDINGS

In the opinion of most observers, a typical Ewing's tumor manifests itself first either in the metaphysis or in the central portion of the shaft when involving a long bone. Even though the roentgenogram may show an apparent involvement of only a portion of the shaft, pathologic specimens usually show that the disease has extended much farther along the center of the bone than was apparent on the roentgenogram. Therefore, it is well to assume that the entire shaft may be involved. The epiphyses are rarely involved and then only as a secondary manifestation.[6] Reactive, non-tumor bone formation is usually de-

FIG. 1. Case 1 (No. 377228). P.P., male, aged fourteen. Admitted because of pain and swelling and interference with function of the right forearm, for the past six months. The swelling was large, irregular, and nodular. Roentgenograms show bone destruction in the lower end of the radius with minimal subperiosteal bone production and a large soft tissue mass. Histopathologically, it was thought to be a reticulum cell sarcoma but later was reclassified as Ewing's tumor. Amputation was done below the elbow. The patient died eighteen months after amputation with metastasis to the chest and brain.

Fig. 2. Case 11 (No. 654461). L.C., male, aged seventy-six. Admitted with dull pain in the right humerus which had become gradually worse since the onset four months before. There was marked limitation in supination of the forearm and all passive motion in any direction caused pain in the upper extremity. A large swelling was seen in the mid-portion of the arm. Aspiration biopsy showed Ewing's tumor. Roentgenograms show a purely destructive lesion with a pathological fracture. He was given 2,200 r over each of two 10 by 12 cm. fields cross-firing the tumor; an estimated tumor dose of 3,500 r was delivered into the tumor. Amputation followed. Postoperative histopathological study showed all tumor cells to have been destroyed. The postoperative course was uneventful and the patient is alive and well nine months after operation.

scribed as predominating over the bone destruction. Peripheral bone thickening and increase in density are usually stressed with central bone destruction considered a relatively late manifestation of the disease.

In this connection, it might be pointed out that two types of new bone formation can be expected from this non-osteogenic tumor. Because of its non-osseous origin, only reactive or non-tumor bone is produced. This may be subperiosteal, in which case it is usually described as characteristically deposited in onion skin-like layers producing a laminated pattern parallel to the long axis of the shaft. It may also be intracortical as the result of a diffuse deposition of new bone within the trabecular structure, creating an increased density in addition to that produced by the overlying subperiosteal new bone. Bone is not formed by the cells of the tumor but bone formation is stimulated when it invades the subperiosteal space and displaces the periosteum outward or permeates the cortex. This is in contrast to osteogenic sarcoma which provokes new bone formation both by osteogenesis by tumor cells and by non-tumor growth. In the latter, the new bone is formed by normal osteoblasts. The rare finding of bone formation in areas of tumor metastases in soft tissues, then, serves to differentiate the true osteogenic tumors.

The successive layers of subperiosteal new bone may be close together or spread rather far apart. When the tumor breaks through one layer it provokes another and

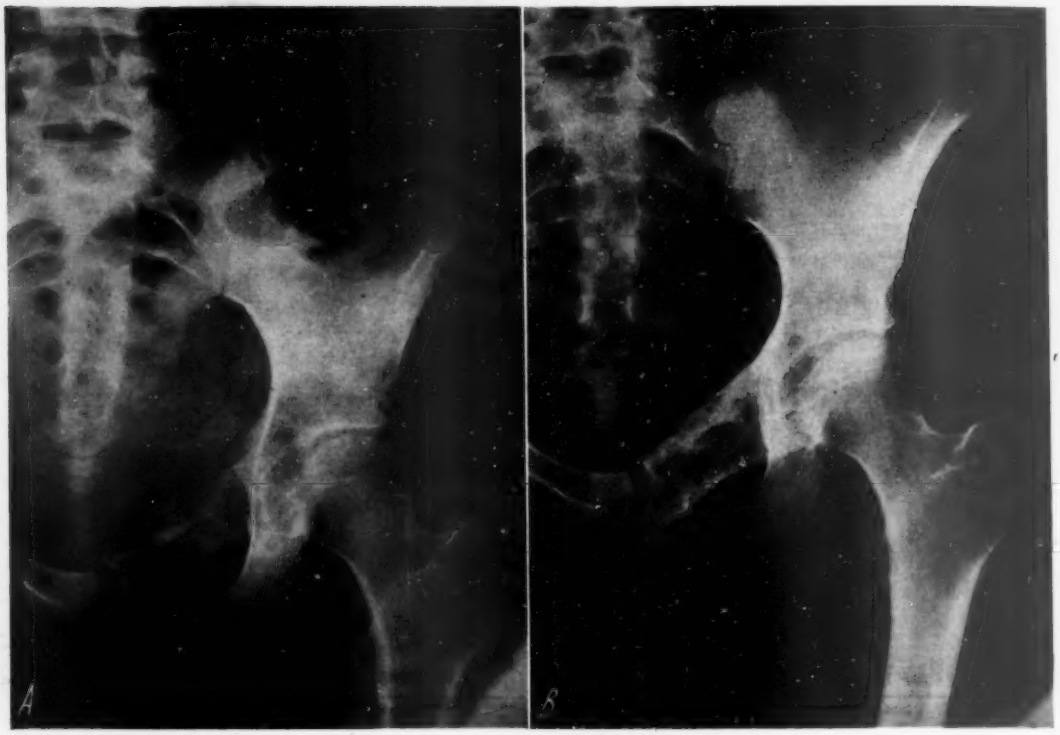

FIG. 3. Case III (No. 461587). C.P., female, aged eighteen. Admitted complaining of intermittent pain in the left hip and pubic region, of two years' duration. There was a definite lump in the groin. *A*, roentgenogram shows an osteolytic, expanding, lesion in the pubis and ischium. Pain was controlled for some time by roentgen irradiation but there was eventual metastasis to the skull, the clavicle, and the spine. *B* shows the recalcification of bone following roentgen therapy. The patient died eight months after admission.

then pushes out the second or third by rapid growth of the tumor tissue between. Soft part involvement beyond the periosteal sheath occurs later, depending on the rapidity of growth. It is this peripheral bone producing character that has often made its differentiation so difficult from a luetic or low grade pyogenic infection.

It has been our experience, however, that the reactive bone production was often conspicuous by its absence except after roentgen therapy had been administered and bone production thereby stimulated as a healing phase in the disease. Indeed, we have found that bone lysis was usually the predominating finding. Of the 26 cases, 16 (62 per cent) showed bone destruction only, 6 (23 per cent) showed minimal bone production, and in 4 cases (15 per cent) bone production was rather an outstanding feature. Only 4 of the 26 cases showed the onion skin-like lamination. Few of the tumors in our series resembled each other except that their malignant nature was apparent. In none of the roentgenograms reproduced in this article can any one pathognomonic finding peculiar to all be found. All of these 26 cases were considered to be Ewing's tumor on histopathologic examination, although the histopathologic picture varied as described elsewhere by Dr. Stout. It is impossible to correlate the variations in the histopathologic structure. Those in the younger age group seem to have more reactive bone formation and in these only was there any suggestion of definite layering of the periosteum. In one of them, the reactive bone was laid down in a more or less perpendicular manner to the shaft resembling somewhat the sun-ray appearance seen in some of the osteogenic sarcomas. It was

more compact and denser, however (Case VII, Fig. 7).

Neely and Rogers[8] interpreted the roentgen evidence obtained in their series of cases as suggesting that the site of origin of the tumor may be the cortex or subperiosteal region. They base this assumption on the fact that in 2 of their advanced neoplasms, the marrow cavity though irregular was visualized throughout the length of the shaft. The marrow cavity was not enlarged as in an expanding tumor of central origin. In contrast to this, we have the impression that the tumor always arises in the narrow. In most of our cases there seemed to be a definite expansion of the cortex. Moreover, it seems not unlikely that the marrow cavity may contain considerable tumor with no demonstrable change in the central negative shadow at the same time that the cortical bone and periosteum show changes due to the permeation of the tumor cells through the haversian canals. Therefore, absence of enlargement of the marrow shadow does not rule out the presence of tumor in the center of the bone and cannot be taken as evidence against a central origin of the neoplasm, since no estimate can be made of the amount of marrow involvement. It is only when sufficient tumor growth is present to produce a defect in the endosteal side of the cortex that one becomes aware of its presence on the roentgenogram. As additional evidence of the central origin of Ewing's tumor, we can point out that when the metaphysis of a long bone is affected, involvement of the cancellous bone in the subepiphyseal zone occurs simultaneously with the involvement of the thin cortex and subperiosteal space in this region.

In only one of the cases in this series was there any question as to the malignant nature of the lesion from the roentgenographic standpoint. This case presented an expanding lesion of the clavicle with minimal production of new bone underneath the overlying periosteum which, for a time, raised the question of a chronic low grade infection. In 3 of the cases in which there was considerable bone production the process was thought to be a probable infection by untrained observers who did not appreciate the malignant invasive features apparent on the roentgenograms. Another had been considered a tuberculosis of the spine until at the time a spinal fusion was performed a biopsy yielded tumor tissue.

Fig. 4. Case IV (No. 530946). A.S., male, aged twenty. Admitted because of throbbing pain in the left sacroiliac region of nine months' duration. The pain was intermittent in character but increasing in severity and radiated down the course of the sciatic nerve as far as the calf and heel, so severe at times that the patient was unable to sleep. Two months before admission the patient noticed a slightly tender lump in the left sacroiliac region. This mass was of rubbery consistency measuring 6 by 8 cm. and was situated over the sacroiliac synchondrosis. No fluctuation was noted. Biopsy showed a definite Ewing's tumor. The roentgenogram shows a destructive lesion in the sacroiliac region with some bone production. Radiotherapy controlled the pain temporarily but the patient died of generalized metastases ten months after admission.

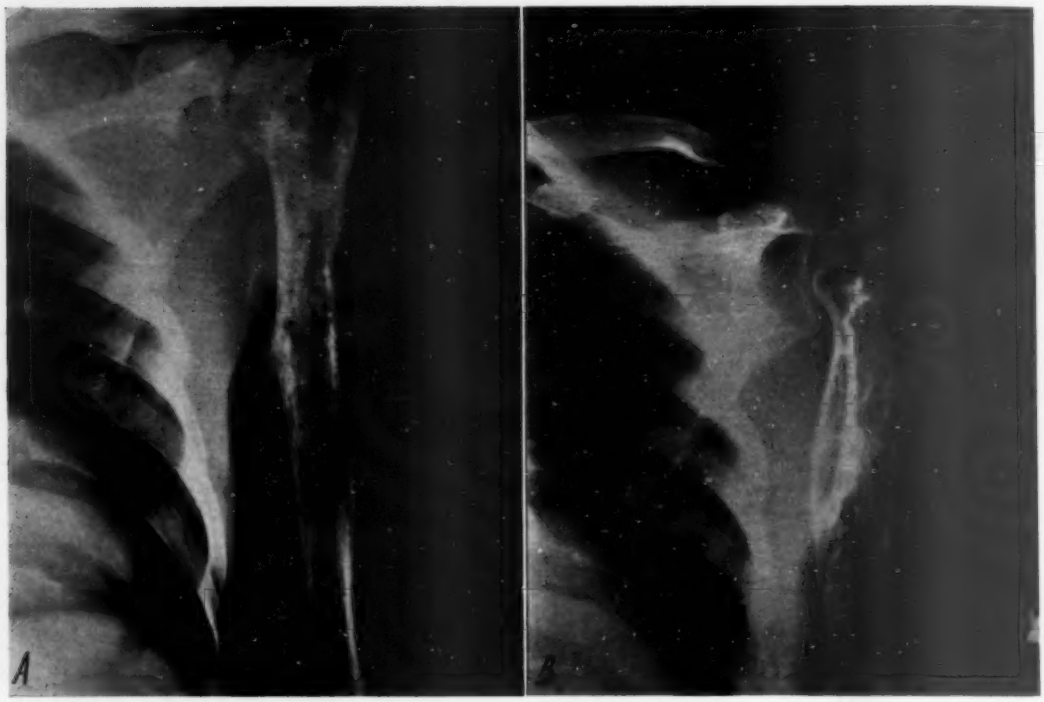

FIG. 5. Case V (No. 44300). V.D., male, aged twenty-five. Admitted in February, 1935, complaining of pain for the past year in the left shoulder. He had been treated for neuritis. Six months before admission he noticed a lump over his shoulder with increasing pain. Biopsy showed Ewing's tumor. *A*, roentgenogram reveals a destructive lesion in the humerus with minimal subperiosteal new bone formation at the periphery of the tumor mass. *B* shows a prompt response to roentgen therapy after an estimated 4,500 r had been delivered into the tumor. The patient died six and one-half years later from pulmonary metastasis.

Once the malignant nature of the disease was recognized, errors were made chiefly in considering the purely osteolytic lesions as probable metastatic carcinoma. One case was considered a lymphosarcoma because of the multiple osteolytic lesions associated with mediastinal adenopathy. A number of cases were considered osteogenic sarcoma, the diagnosis of Ewing's tumor being made after biopsy. Thus it is evident that although there will be suggestive roentgenographic and clinical differential features in some instances, biopsy will have to be the deciding factor in all.

THERAPY

Our material is obviously too meager to permit any definite conclusions to be drawn in regard to the best method of treatment, when compared with other larger groups studied.[1,2,7] There are nevertheless certain pertinent observations to be made from individual cases which may be helpful in the treatment of future cases.

The efficacy of radiation therapy can be judged only from the cases of more recent years and then only in those in which we can be reasonably certain that the therapy judged by our present standards was adequate. One case, with the disease in a vertebral body, treated by irradiation alone, is alive and symptom free in the sixth year. Another was arrested for six years by irradiation alone only to succumb in the seventh year from pulmonary metastasis. A five year period of observation is therefore too short to determine whether the disease has been eradicated. One patient is well thirty-two years following amputation of the involved extremity.

In those cases adequately treated an attempt was made to cross-fire the lesion

TABLE I

EWINGS' TUMOR OF BONE MARROW
PRESBYTERIAN AND BABIES HOSPITAL CASES (1908–1942)

Patient	History	Sex	Age	Bone	Surgery	Radiation Treatment	Surgery + Radiation	Result
H. J.	8236	M	21	Femur	+			32½ yr. well
T. M.	14709	F	17	Femur	+			4½ mo. died
E. R.	17686	F	44	Tibia	?	?	?	No follow-up
M. L.	20069	F	4	Maxilla	+			No follow-up
J. D.	23472	M	17	Maxilla		+		6 mo. died
H. L.	30662	M	21	Ilium		+		7 mo. died
M. H.	33055	F	40	Sternum	?	?	?	15 mo. died
A. M.	37970	M	40	Ilium		+		11 mo. died
P. F.	58948	M	15	Femur	+			6 mo. died
E. W.	76098	F	18	Rib			+	12 mo. died
E. D.	84777	M	19	Rib		+		8 mo. died
C. D.	257772	M	23	Clavicle		+		8 mo. died
M. H.	317928	M	31	Scapula	+			2 mo. died
A. J.	329325	F	32	Temporal		+		? 12 mo. died
P. P.	377228	M	14	Radius			+	18 mo. died
J. H.	403761	M	6	Humerus			+	27 mo. died
V. D.	443000	M	25	Humerus		+		75 mo. died
C. P.	461587	F	18	Pubis		+		8 mo. died
T. K.	527731	M	14	Vertebra		+		76 mo. alive
A. S.	530946	M	20	Ilium		+		10 mo. died
R. H.	605649	M	7	Humerus		+		18 mo. died
L. M.	290808	F	16	Mandible		+		22 mo. alive
L. C.	654461	M	76	Humerus			+	(recent) alive
G. G.	662419	F	33	Rib		+		(recent) alive
L. F.	666778	F	79	Parietal		+		(recent) alive
H. H.	410666	F	15	Rib		+		13 mo. died
Totals					5	15	4	

from every possible angle and make the field of irradiation large enough to include a much greater area than the apparent amount of bone involvement, roentgenographically, would indicate. The quality of the roentgen-ray beam used is probably of importance only insofar as it may be necessary to vary its penetrating power. Both 135 kv. and 200 kv. roentgen rays were used in treating these cases, depending on the thickness and position of the part involved. Daily doses varied in amount, de-

TABLE II

ANALYSIS OF ROENTGEN FINDINGS

Cases	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17*	18	19	20	21	22	23	24	25	26	Total
Bone destruction	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	+	+	o	+	+	+	+	+	+	24
Increased density within the bone	+	+	o	o	o	+	o	+	o	o	o	o	o	o	o	?	o	o	+	o	o	o	o	o	o	o	5
Increased width (expansion)	o	+	o	o	+	o	+	o	+	+	o	+	o	o	o	?	o	o	+	o	o	o	o	o	o	+	8
Subperiosteal new bone	o	o	o	o	+	o	+	+	+	+	+	+	o	+	+	?	o	o	+	o	o	o	o	o	o	o	11
Layering effect	?	o	o	o	+	o	+	o	+	o	?	+	o	o	o	?	o	o	o	o	o	o	o	o	o	o	4
Soft tissue tumor mass seen roentgenographically	?	o	+	o	+	o	+	o	+	o	+	o	o	+	o	?	o	o	o	o	o	o	o	+	o	o	7

* Indeterminate old cases with incomplete description—roentgenograms no longer available.

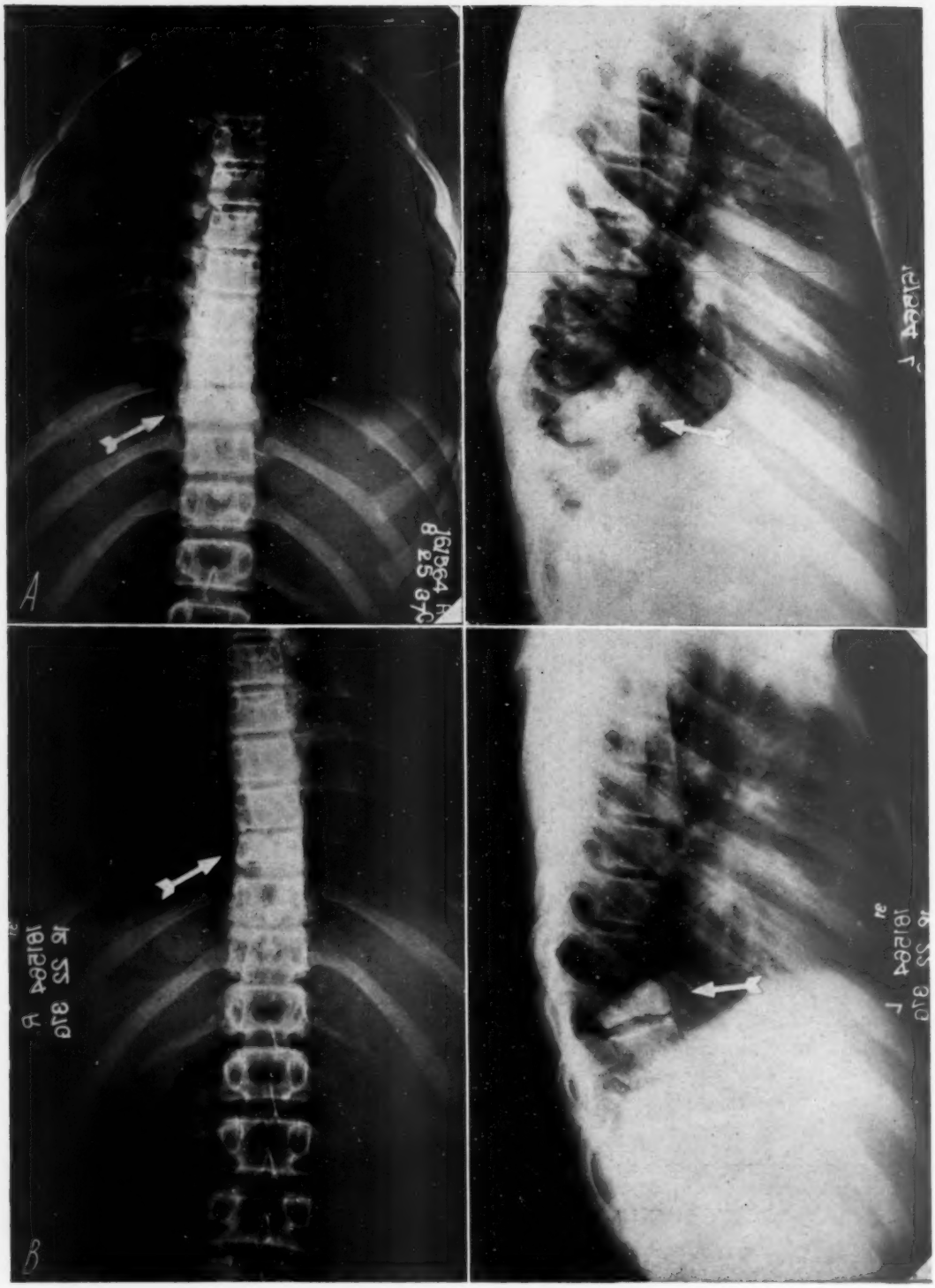

FIG. 6. Case VI (No. 527731). T.K., male, aged fourteen. Admitted in July, 1937, complaining of constant, non-radiating pain in the thoracic spine, of five months' duration. Pain was worse on movement and at night. Roentgenogram (*A*) show a destructive lesion with wedging of the ninth dorsal segment and a paraspinal soft tissue shadow. A fusion operation had been done at another hospital because the condition had been thought to be tuberculosis. Biopsy showed Ewing's tumor. Intensive roentgen therapy apparently arrested the tumor and the patient is alive and well today, in the sixth year. Lesion is shown following therapy (*B*).

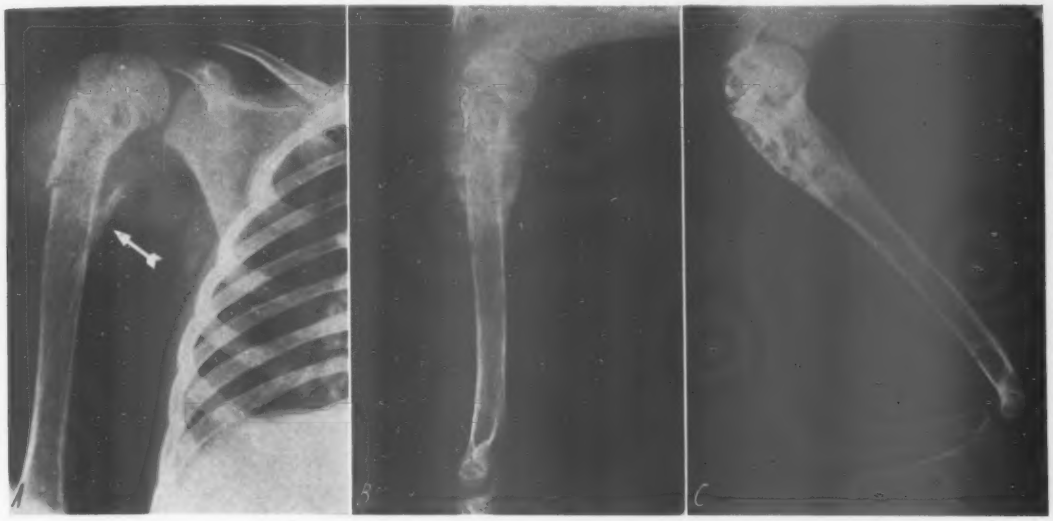

Fig. 7. Case VII (No. 605649). R.H., male, aged seven. Admitted because of pain and swelling of the right shoulder of five months' duration. There was progressive limitation of motion of the arm. Roentgenogram (*A*) shows a destructive lesion in the upper end of the humerus with considerable new bone formation, the pattern of which suggested osteogenic sarcoma because of the striated subperiosteal new bone laid down perpendicular to the long axis of the shaft. There is also onion-skin layering at the periphery of the tumor at arrow. The patient was given 3,500 r (measured in air) over each of two fields, anterior and posterior, including the entire arm and shoulder. There was a prompt initial response but later metastases developed in the forearm, the tibia, lungs, and brain. Roentgenograms (*B*) and (*C*) show shrinkage and recalcification of tumor four and six months after roentgen therapy.

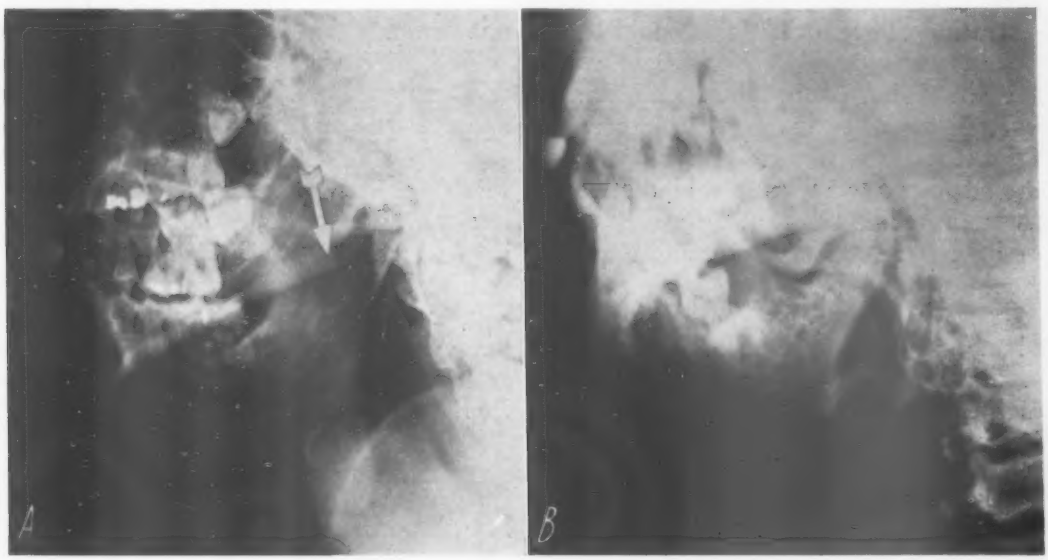

Fig. 8. Case VIII (No. 290808). L.M., female, aged sixteen. Admitted because of swelling of the left side of face of two months' duration. The mass has been steadily increasing in size. Opening the mouth produced a tickling sensation and chewing occasionally produced pain. A robin's egg shaped, hard, non-tender mass was found fixed to the deep structures overlying the left preauricular region. The regional nodes were not enlarged. Roentgenogram (*A*) shows bone destruction in the mandible without bone production. Biopsy showed Ewing's tumor. There was prompt response to roentgen therapy (*B*). The patient is alive and well twenty-four months after admission.

pending on field size, and age, and tolerance of the patient.

A study of pathologic specimens may show that, as mentioned above, the disease can extend through the soft tissue of the marrow without producing recognizable changes in bone density. It should be assumed, therefore, for the purpose of roentgen therapy, that the entire bone is involved. If a lesion is present in the upper end of the humerus, for example, the entire shaft should be intensively irradiated. The lesion should be cross-fired from as many directions as necessary, in an attempt to get a maximum dose of about 4,500 r delivered into the tumor. In one recent case (Case II, Fig. 2), the humerus was amputated after irradiation and histopathologic examination showed the specimen to be free of all tumor tissue. Necrotic material had replaced the entire tumor mass. The total tumor dose in this instance approximated only 3,500 r. Much less has been used with complete arrest. Case VI, alive and well in the sixth year, received an estimated tumor dose of 2,700 r. The administration of such a large tumor dose as 4,500 r is not possible of course in cases where the lesion cannot be as efficiently cross-fired as in an extremity. In certain locations the danger to important soft tissue structure, such as the bladder and intestine, must be taken into consideration and the dosage regulated accordingly. In the child, possible injury to the growth centers must be considered while treating the bone but this danger cannot affect the plan for treatment too much since the growth disturbance resulting can be overlooked in the face of a life saving procedure.

The regional lymph nodes should be irradiated when they are clinically suspected of involvement even though histopathologic proof is lacking. In only 3 of our cases, however, were the regional nodes described as palpable, though not proved to contain tumor by section. Geschickter and Copeland[6] give the regional nodes as the third most common site of spread of the disease.

Inasmuch as the tumor is usually radiosensitive in all its variations, it seems reasonable to give preoperative irradiation if and when amputation is to be done. In view of the case cited above where complete sterilization of the tumor mass was obtained before amputation in a relatively short time, it seems logical to proceed along this plan. Had Case V (Fig. 5), who died in the seventh year following irradiation, only been subjected to subsequent amputation his chance of survival might have been improved.

Metastases must be treated as they appear, but we have found that the metastases and recurrences are usually not as radiosensitive as the primary lesions. Once the tumor has metastasized to the soft tissues or is originally recognized as multiple foci in the skeleton, only palliative treatment should be given, no attempt being made to give a dose which will completely destroy the tumor.

Coley's toxin was given to 3 of the earlier cases in our series but the results cannot be evaluated because we do not know whether the proper type of toxin was used, nor whether the dosage was properly controlled. Included in these three is the one patient well thirty-two years after amputation of the involved extremity.

CONCLUSIONS

1. Ewing's tumor shows great variations in its roentgenologic manifestations as well as in its histopathologic picture.

2. Because of these variations, there is no typical roentgen picture of this disease and a definite diagnosis can rarely be made from the roentgen examination alone.

3. The disease may spread from the area of obvious primary involvement throughout the soft tissue of the marrow cavity without producing bone destruction which would betray its entire extent. It is important to take this fact into consideration in planning roentgen therapy.

4. Though arrest of the disease has been reported from either surgery or roentgen therapy alone, the evidence suggests that a combination of the two methods

when possible will probably give the best results.

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DISCUSSION OF PAPERS BY DRS. STOUT AND SWENSON

Dr. George W. Grier, Pittsburgh, Pa. I am sorry that Dr. Ewing isn't here this morning because I remember very well two previous occasions on which this subject has been discussed before this Society and on the last occasion in particular Dr. Ewing spoke quite emphatically. He said that the Ewing tumor was his child, and if he didn't know what it was, he would like to know who had a better right to describe the Ewing tumor. Now he may have changed his mind about the Ewing tumor, I don't know, but certainly what he said the last time he spoke before this Society seems to me to be an exact contradiction of what has been said here this morning.

I remember perfectly well that Dr. Ewing said that if the diagnosis had to be made either by microscopic examination or by roentgen film, he would choose the film. He said that very definitely before this Society and yet what has been said here this morning is just the opposite. I know nothing about microscopic diagnosis, but I remember very well the way Dr. Ewing described his tumor and he called it an angio-endothelioma, which perhaps is unfortunate, because it has been my experience—and I have had this experience many times since Dr. Ewing spoke—that the pathologists recognize as angio-endothelioma something entirely different from what Dr. Ewing described. Dr. Golden described this typical onion-skin appearance which has been referred to here this morning as new bone laid down outside the bone, but if one will read a book entitled "Bone Sarcoma" written by the Committee on the Registry of Bone Sarcoma of the American College of Surgeons, Drs. Codman, Bloodgood and Ewing, it will be seen that they say that the tumor cells are laid down in layers between the structure of the bone, not on the outside of the bone but on the inside of the bone, and these onion-skin layers are not new bone laid down on the outside. They are layers of bone that are pushed apart by these layers of new growth cells. That is what they say in this book and that is what Dr. Ewing said when he spoke on this subject before this Society, and he insisted that unless that effect were present, it was not a Ewing tumor regardless of what the microscopic appearance was.

I should like to ask Dr. Golden if he knows whether Dr. Ewing has changed his mind on this subject, because since it is his tumor I am inclined to accept his description of it. If he has changed his mind about it, I think we should know. Most of the cases that were shown here this morning were not that type. They were probably angio-endotheliomas, I suppose, but certainly a different tumor entirely from what Dr. Ewing insisted was his tumor.

Dr. Maurice Lenz, New York. Dr. Swenson, were he present, would probably agree that a tumor dose of 4,000 to 4,500 r would be considered adequate in a Ewing's tumor. It is difficult to decide whether surgery or roentgen therapy is preferable in a given case, if the tumor can be removed. Amputation would seem to be advisable if the soft tissues around the bone have not been invaded, if the disease is in the distal portion of an easily removable extremity, and if there is no evidence suggesting metastases. In the present series, only 2 cases were well after five years; one had been treated surgically and the other by roentgen therapy. A third one lived over six years following roentgen therapy without surgery.

DR. CHARLES L. MARTIN, Dallas, Texas. If I understood Dr. Stout's paper correctly, he sometimes finds if difficult to differentiate the microscopic picture of Ewing's tumor, reticulum cell tumor and neuroblastoma. I have encountered this difficulty and might add myeloma to the list. The intermixture of some of these neoplasms might explain the discrepancies in the appearance of the roentgenograms presented.

DR. ROSS GOLDEN, New York (closing). I am "on the spot" because I am not a pathologist and cannot answer questions about pathology. However, in his text, it is clear that Dr. Stout does not include neuroblastoma and reticulum cell tumors with Ewing's tumor, but some cases of Ewing's tumor contain reticulum cells.

This discussion emphasizes the remark made in Dr. Stout's opening paragraph, that this is a very disputable tumor.

Dr. Grier says that many of the cases shown in this presentation were not Ewing's tumor because the films did not show the "typical" appearance described by Dr. Ewing as Dr. Grier remembers it. Presumably he refers to the well known "onion skin" or lamellated appearance. Some of the tumors without the "onion skin" effect have the same histopathologic structure as those with it. Are the former to be considered as something other than Ewing's tumor for that reason? Certainly they acted like Ewing's tumors and were so interpreted by competent pathologists. Inasmuch as Dr. Stout is not here, I will ask him to write a reply to Dr. Grier's criticism.

Two points brought out in these papers are worthy of re-emphasis, namely, that there is no correlation between the histopathologic variants of Ewing's tumor and the roentgenologic manifestations, and that there is no such thing as a "typical" Ewing's tumor because many, perhaps a majority, do not show the layering effect of subperiosteal new bone, requiring the diagnosis to be made or confirmed by histologic study of a biopsy.

In regard to roentgen dosage, it is of interest that one patient of Dr. Swenson's series received a tumor dose of approximately 4,500 r in the humerus in March and April, 1935, plus some more later that same year and in 1938. He died of pulmonary metastases in 1941, six years later, without showing clinical evidence of irradiation injury to the bone. He died at home without necropsy. However, the possibility of radiation osteitis must be borne in mind when large doses are given to bones.

DR. ARTHUR PURDY STOUT, New York. In reply to the discussion of Dr. Grier, Dr. Ewing in the fourth edition of "Neoplastic Diseases" published in 1940 makes this statement on page 366: "New bone may be laid down by the periosteum in very characteristic parallel lines or irregular deposits. . . " If Dr. Ewing made the statement credited to him by Dr. Grier "that these onion-skin layers are not new bone laid down on the outside," it would seem that he no longer holds this opinion.

I think we may infer that Dr. Ewing does not believe that unless parallel layering of bone is present a tumor is "not a Ewing tumor regardless of what the microscopic appearance was" for the illustrations used in "Neoplastic Diseases" do not show this layering effect and no such statement appears in the text.

If, as Dr. Grier says, Dr. Ewing asserted that he would prefer a roentgenogram to a microscopic slide in diagnosis, I have not found it recorded in print. I can only say, if that is his opinion, I do not agree with it.

Dr. Ewing has expressed his views regarding the tumor which bears his name in the fourth edition of his book. They correspond with those given in his letter to me and I trust have been faithfully reflected in the text of my paper. With the exceptions noted in that paper I am in agreement with Dr. Ewing's most recent published statements. In general, these do not correspond with Dr. Grier's recollections.

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EOSINOPHILIC GRANULOMA OF THE TIBIA

CASE REPORT

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THE interpretation of this osseous lesion as a granuloma was reported, independently, from three laboratories in 1940 (Lichtenstein and Jaffe,[7] Otani and Ehrlich,[10] and Hatcher[4]). The lesion had appeared previously in the literature under a variety of headings (Finzi,[3] Mignon,[9] and Schairer[11]). Eosinophilic granuloma of bone presents itself as a well localized lesion that begins in the medullary cavity and expands, eroding and even perforating the cortex at the site of the lesion. Its diagnosis is to be suspected in a child or young adult, with a history of painful, localized and rapidly increasing swelling of only a few weeks' duration, and roentgenographic evidence of a rarefied and destructive lesion involving one or more bones (the calvarium, ribs, or long bones), perhaps with pathologic fracture or perforation of the cortex and the formation of a palpable soft tissue mass. There is not infrequently an eosinophilia in the differential white blood cell count, but all other clinical laboratory findings are uniformly normal.

The pathologic picture is distinctive and unlike that of any other known lesion of bone. Grossly, the bone is replaced by a more or less soft, yellowish or brownish tissue. Microscopically, the non-osseous material is composed of a cellular stroma, densely infiltrated by large aggregates of eosinophilic polymorphonuclear leukocytes. The stromal cells are compact, tumor-like aggregates of large cells with pale-staining nuclei and cytoplasm, and there is an appreciable number of large multinucleated cells, resulting from coalescence of the basic proliferating stromal cells, that are distinctly phagocytic and contain eosinophilic and blood pigment granules. Although areas of focal necrosis may be observed, there are none of the usual evidences of bacterial inflammation or suppuration. The osseous fragments show the tumor infiltrating the intertrabecular spaces.

Despite the apparently aggressive nature of the lesion, its excision, with or without roentgen therapy, appears to lead to local relief of symptoms without local recurrence of the growth.

CASE REPORT

A twelve year old Italian male complained of pain in the left midleg of four weeks' duration. There was no history of trauma or preceding infection. Examination revealed swelling and localized tenderness in the midportion of the anteromedial surface of the left tibia, without evidence of discoloration of the skin or local heat. The temperature, pulse and respiratory rates were normal. Clinical laboratory

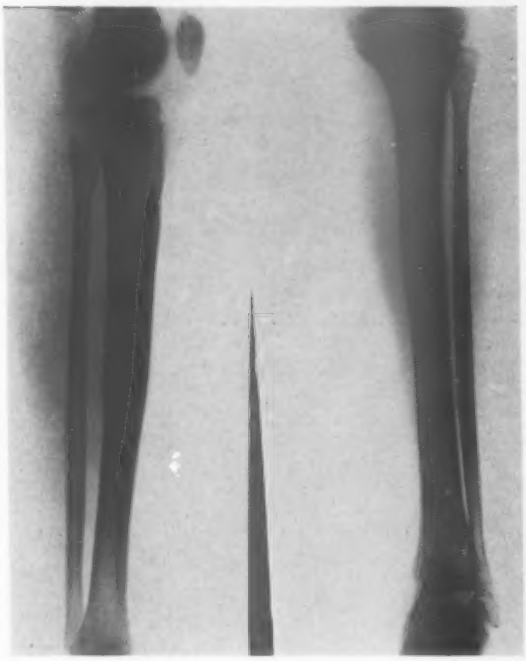

FIG. 1. Roentgenograms of the left tibia demonstrate an oval-shaped, radiolucent area in the midshaft with erosion of the cortex on the medullary side and thickening of the cortex on the periosteal side.

tests, including blood Wassermann and Kahn tests and the intradermal tuberculin test, were negative. The blood sedimentation rate and repeated urinalyses were normal. The blood picture showed 90 per cent hemoglobin, 4,500,000 red blood cells, and white cell counts varying between 5,000 and 8,800. The differential white blood cell count was normal except that the number of eosinophiles varied between 2 and 3 per cent.

Roentgenograms of the left tibia demonstrated an oval-shaped, radiolucent area in the midshaft with erosion of the cortex on the medullary side and thickening of the cortex on the periosteal side (Fig. 1). Comparison of these films with similar roentgenograms taken two weeks previously showed a rapid increase in the size and demonstrability of the osseous lesion. No other lesions were evident in roentgenograms of all the remaining bones of the body.

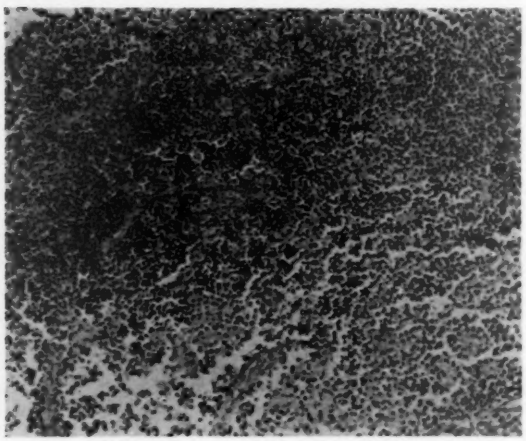

FIG. 2. Photomicrograph (×125) of a section of the non-osseous tissue, demonstrating the masses of eosinophilic polymorphonuclear leukocytes infiltrating the very cellular stroma.

At operation, the thickened cortex over the tumor was removed and the soft, reddish-brown tissue that filled the medullary cavity was excised. In the mistaken impression that the lesion represented a pyogenic osteomyelitis, the surgeon packed the wound with vaselinized gauze and immobilized the limb in plaster of paris. Healing occurred by secondary intention. Growths of *Staphylococcus albus* and *Streptococcus nonhaemolyticus* (probable contaminants) were obtained from the wound. The patient has experienced no further local discomfort, the osseous lesion appears to be healing, and, thus far, there has been no clinical or roentgenographic evidence of the development of new bone lesions.

Histopathologic Features. The microscopic picture of the non-osseous tissue demonstrated the specific features of an eosinophilic granuloma. The masses of eosinophilic polymorphonuclear leukocytes that infiltrated the very cellular stroma constituted the predominating feature. There was a substratum of compact, fairly large cells with pale-staining nuclei and cytoplasm, some of which were multinucleated. Many of these large cells contained eosinophilic and blood pigment granules. There was no distinct abscess formation or other indication of active suppuration (Fig. 2 and 3).

DISCUSSION

The histopathologic features of this lesion are unlike those of any classified disease of bone, either inflammatory or neoplastic. Lichtenstein and Jaffe,[7] Otani and Ehrlich,[10] and Hatcher[4] have considered this lesion as a granuloma of indeterminate origin, and this interpretation has been accepted by Mallory,[8] and Bass.[1] These authors have found no substantiation of the concept that the lesion might represent a myeloma or an osteomyelitis. Cultures of the lesion have been uniformly sterile. Although the granuloma in these reports was solitary, Lichtenstein and Jaffe[7] suggested that the lesion might be the local expression of a systemic response to some etiologic agent or factor, possibly a virus, basing this concept on the finding of active myelopoiesis as reflected by the eosinophilia in the blood smears in many of the reported cases and the finding, in their case, of an increased proportion of eosinophilic myelocytes and young eosinophilic granulocytes in the sternal bone marrow. This impression has been further substantiated by their experience with a case that demonstrated, roentgenographically, lesions in three ribs and both femora, two of the lesions having been exposed and showing the histopathologic features of eosinophilic granuloma.[5]

The interpretation of eosinophilic granuloma as a new and separate disease entity has been challenged by Farber[2] who prefers

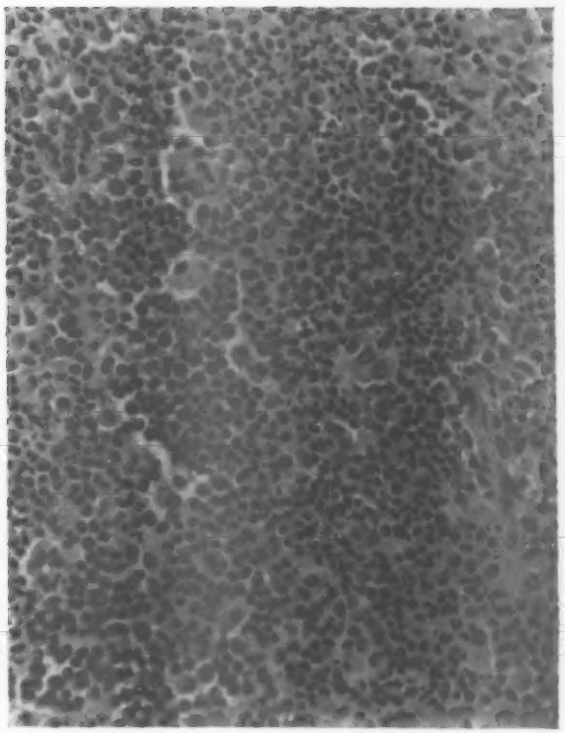

FIG. 3. Higher magnification (×250) color photomicrograph from a densely cellular area in Figure 2, showing the large number of eosinophilic polymorphonuclear leukocytes. There is a substratum of compact, large, pale-staining cells, some of which are multinucleated. Many of these stromal cells are filled with phagocytosed eosinophilic and blood pigment granules.

to consider this lesion of bone, and the osseous and visceral lesions of Hand-Schüller-Christian's disease, as representing variations in degree, stage of development and localization of the same basic disease process. According to Jaffe[5] and Lichtenstein,[6] this resemblance is superficial and the interpretation of the lesion, herein discussed, as a lipogranuloma is not acceptable under existing evidence. In both conditions, children or very young adults are affected, and there may occur osteolytic lesions in the calvaria. Their clinical courses are quite different, however, and their pathologic anatomy is wholly dissimilar according to those who understand the histopathologic features in both conditions. For example, large collections of foam cells, fibrous tissue reaction, and walling-off reaction of the surrounding bone are not demonstrable in eosinophilic granuloma of bone as they are in the lesions of Hand-Schüller-Christian's disease. The macrophages that constitute a conspicuous feature in the former lesion and that often contain phagocytosed eosinophiles, red blood cells, and eosinophilic and blood pigment granules, are not essentially lipophilic. Although these cells may contain a small number of lipoid granules there is no evidence of doubly refractile fat.

CONCLUSIONS

An instance of eosinophilic granuloma involving the tibia of a twelve year old male is reported. No other bones demonstrated the lesion, roentgenographically. The differential white blood cell count revealed a mild eosinophilia. Attention is directed to the specific histopathologic features of this lesion that are unlike those of any classified disease of bone.

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THE OPTIMUM KILOVOLTAGE TECHNIQUE IN MILITARY ROENTGENOGRAPHY

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MILITARY roentgenography requires standardization of apparatus and technique in order that all operations employed will entail a minimum of time and yield results of the best quality. To that end, the training of Army roentgen-ray technicians involves the problem of providing the student technician such basic instruction as will fit him to perform satisfactory routine roentgenography irrespective of the military assignment.

The results of the beginner, whether good or poor, usually are unintelligible to him. For that reason he must early be made acquainted with the kind of roentgenogram that is most useful to the roentgenologist—one that possesses correct diagnostic quality. The student cannot acquire that knowledge except by actually making such roentgenograms under careful guidance. His familiarity with satisfactory roentgenograms based on experience in making them, instills in him immeasurable self-confidence that is a valuable asset in the field or elsewhere. It makes possible a further development of roentgenographic aptitude invaluable in every laboratory.

To facilitate this training, a simple, though exact exposure system—the *optimum kilovoltage* technique—has been developed which requires little applicatory effort on the part of the technician. Wherever practical, the exposure factors are reduced to constants, thereby eliminating many possible sources of error. This system enables the student to quickly become acquainted with better-than-average quality roentgenograms that are produced in the course of instruction. It precludes his floundering about, seeking exposure factors for making a particular roentgenogram whose quality he is totally incapable of judging.

The fact that military necessity requires the elimination of non-essentials or variables from the technical procedure accounts for the success of the optimum kilovoltage technique, since it provides a clear-cut method of procedure, assures the production of better-than-average results, and is easily understood and applied by the beginner and the experienced technician alike. The technique is adaptable to a speedy, efficient roentgenographic routine, and is applicable not only in laboratories having fixed installations, but also in the changing conditions imposed by unpredictable military situations in the field.

The variety of injuries encountered in military roentgenography requires that the patient be subjected to the least possible manipulation. Also the fact that many parts are bandaged, splinted, or placed in casts, makes out of the question recourse to laborious techniques requiring the measurement of the part and computations for the determination of the proper exposure factors.

The optimum kilovoltage technique does not require actual measurement of the body part. With some experience, the technician learns to *estimate* the thickness and is able to classify the part as *small*, *average*, or *large*. Since the *average* classification predominates, he may successfully place about 90 per cent of all patients in this category. The basic constants of kilovoltage and milliampere-seconds are so few in number that they are easily memorized. For ready reference, the factors may be placed on a small card. For military technicians, the technique will be found exceptionally useful, where speed is essential and surety of results particularly necessary.

The employment of the optimum kilovoltage technique will consistently produce

roentgenograms of good quality with a minimum of effort and with the simplest of apparatus. Since the method is standardized, shifting of personnel from one laboratory to another should not interfere with the uniformity of results; each technician trained in its use should produce the same quality and type of roentgenograms that his predecessor did. The roentgenographic densities produced by this method are uniform—a point of considerable diagnostic value because any differences from the normal density may be attributed to pathological change within the tissues. Duplication of results is easy to attain in follow-up cases.

The technique may be employed with any type of rectified or self-rectified apparatus if the apparatus is capable of providing at least 30 ma. and 85 kv. (peak). It is particularly applicable to the U. S. Army Field X-ray Unit (Item 96085). Its success in the training of over 600 students in the X-ray Section, School for Medical Department Technicians, Army Medical Center, has been proved by the quality of roentgenograms made not only in the School, but also in the far-flung locations where many of our technicians are now on duty.

THE OPTIMUM KILOVOLTAGE TECHNIQUE

The tendency in present day roentgenography has been the injudicious use of high milliamperages to perform work they are not always capable of performing. It must be understood that for a given thickness of a particular body part, the wave length of the roentgen rays employed to penetrate the tissues must be adequate or, in other words, *optimum*. Since the kilovoltage governs the wave length and penetration, all that is then necessary to secure a satisfactory image is to have a sufficient number of roentgen rays reach the film. The milliamperage and time controls the *number* of roentgen rays or intensity of radiation, and proper adjustment of these factors will produce adequate exposure of the roentgen film. When the roentgen-ray wave length is optimum, a lesser amount of milliampere-seconds is usually needed for the exposure than that habitually employed for the same purpose with lower kilovoltages. This is most important where conservation of tube life is necessary, for it is milliampere-seconds that commonly destroys tubes—not kilovoltage. Fewer milliampere-seconds, of course, will permit a greater number of roentgenograms to be made over a given area before the limit of radiation safety is reached. Obviously, in many instances, the need for the higher milliamperage apparatus is precluded, provided attention is paid to the proper use of kilovoltage.

The optimum kilovoltage technique developed by the author over a period of years is based upon the above concept and its successful use entails only an acceptance of a few basic principles relating to the production of the roentgenographic image. In the interest of brevity, these data are listed below (a detailed exposition of the subject will be published in the near future).

Roentgenographic Image. The roentgenographic image is a pictorial record or representation of the internal elements of body tissues traversed by a beam of roentgen rays. It comprises what is more commonly known as *roentgenographic detail.* In an analysis of the image, two aspects must be considered: the *geometric aspect* which influences the *formation* of the image as to its sharpness, degree of magnification, etc., and, the *photographic aspect* which influences the reproduction or *recording* of the image on a roentgen-ray film. It is the latter aspect upon which the optimum kilovoltage technique is based.

Roentgenographic Density. In order for an image to be distinguished on a roentgen-ray film, differences in the opaqueness to transmitted light of the deposits of black metallic silver must be present on the film. These various deposits constitute the image and are known as *roentgenographic densities.* The gradations and degrees of translucence of these densities depend upon the various intensities of radiation reaching the film after having penetrated the body

tissues. Image details are differentiated on the roentgenogram by the *differences* in density or the varying degrees of translucence presented by each density to the light from a standard roentgen-ray illuminator. Each density has a certain degree of translucence; that is known as its *tone value*. The gradations of densities or tones may be few or many and is described best by the term *roentgenographic contrast*.

Roentgenographic Contrast. Roentgenographic contrast becomes evident when a visual differentiation between densities on the roentgenogram is made; it is accomplished by comparing the translucence of one tone density with another. When the range of tones is small and the transition from one tone to the next is abrupt (great density difference), the roentgenogram is said to exhibit a *short scale* of contrast. When the range of tones is extensive and the transition is gradual, the roentgenogram has a *long scale* of contrast.

The influence of various exposure factors upon these photographic aspects of the image is as follows:

Kilovoltage. When roentgen rays are produced for the purpose of making a roentgenogram, the *quality* of the roentgen rays (*wave length*) must be approximately predetermined. Since kilovoltage determines the wave length of the roentgen rays it also dictates the degree of *penetration* that can take place. In every instance, the wave length must be such as to *adequately penetrate* the part. The lower the kilovoltage, and the longer the wave length, the less penetrating the roentgen rays; the higher the kilovoltage, and the shorter the wave length, the more penetrating the roentgen rays.

Kilovoltage influences the generation of *secondary radiation* which is produced in the body tissues by primary radiation; its wave length is longer than that of the primary beam. Much of the secondary radiation is absorbed by the tissues themselves but, under certain circumstances, some of it passes from the tissues to expose the roentgen-ray film. Since secondary radiation is unfocussed, it tends to obscure detail by superimposing a *supplementary* density on the image, commonly known as secondary radiation fog. It creates an *unwanted* density on the film, and every means should be employed to eliminate or reduce it to a minimum. The lower the kilovoltage, the less the amount of secondary radiation produced; the higher the kilovoltage, the greater the secondary radiation.

Kilovoltage influences roentgenographic contrast directly. The lower the kilovoltage, the shorter the contrast scale, and *less* detail is visible; the higher the kilovoltage, the longer the scale of contrast, and *more* detail, within certain limits, is visible. When it is desired to record a large number of tissue densities, it is necessary to employ one of the higher kilovoltages so that long scale contrast is secured. Small differences in tissue density are then rendered as small roentgenographic density differences in the image, thereby aiding in detail differentiation.

By its control over contrast, kilovoltage also determines the *exposure latitude* of the roentgen-ray film emulsion. Exposure latitude is that film characteristic which, by reason of the existing contrast scale, determines the spread or extent of exposure, or interval, between the least and the greatest exposure that will produce a satisfactory image. When optimum kilovoltages are used the latitude is sufficiently great to permit either halving or doubling the milliampere-second value to obtain the desired density for each thickness classification of patient.

Obviously, when the contrast scale is short, the margin of permissible error in exposure is very limited and the time of exposure must be critically determined. On the other hand, long scale contrast makes it possible to take advantage of the extremely great exposure latitude of the roentgen-ray film, wherein a greater range of exposure may be made without detriment to the diagnostic quality of the roentgenogram than does short scale contrast. Furthermore, the exposures need not be critical. This great

latitude in exposure that characterizes the use of the higher kilovoltages makes practicable the optimum kilovoltage technique.

Milliampere-Second Factor. When employing an optimum kilovoltage for a given part, the milliampere-second (ma-sec.) factor will determine directly the intensity or *quantity* of radiation reaching the roentgen-ray film. It represents the product of milliamperage (ma.) and exposure time in seconds (sec.). There is an interrelationship between it and the anode-film distance, but since distance is more or less a constant, the milliampere-second factor can usually be considered the dominant factor influencing intensity. (It is assumed that adequate adjustment of the milliampere-second factor is made when the distance is changed for a given projection.)

The quantity of radiation reaching the roentgen-ray film after passage through the tissues determines the density of the image. In other words, roentgenographic density is directly proportional to the intensity of radiation reaching the film. Therefore, the milliampere-second becomes the controlling factor in the production of roentgenographic density.

"Heel Effect" of Tube Anode. A beam of roentgen rays emitted from the focal spot of the tube is not homogeneous in its intensity. It has been found by sensitometric measurement that the roentgenographic densities vary considerably at various points on a roentgenogram in an axis parallel to the long axis of the tube. This indicates that the intensity of the cathode portion of the roentgen-ray beam shows a slight increase as compared with that of the central ray. Conversely, the intensity shows a gradual progressive decrease from the central ray toward the anode side of the beam and there may be a loss of intensity at the limit of the anode side of the beam of as much as 70 per cent. The effect is more apparent when employing a tube with an anode slope of 15° than one with a 20° anode slope and also when employing the shorter anode-film distances; but it diminishes as the anode-film distance is increased. Thus, the variation in intensity makes it possible to balance roentgenographic densities by taking advantage of this inherent characteristic of all roentgen-ray tubes.

To balance roentgenographic densities on a roentgenogram, the "heel effect" of the tube anode should be employed by adhering to the following rule:

> *Align the long axis of the tube parallel to the long axis of the part and direct the cathode portion of the roentgen-ray beam toward the area of greatest tissue density.*

For example, in roentgenography of the entire leg on a 14×17 inch film, the long axis of the tube is aligned parallel with the long axis of the leg and the cathode portion of the roentgen-ray beam is directed toward the proximal portion of the leg.

Screens, Cones, and Grids. Intensifying screens of medium speed have been found best for standardization of technique since their relatively small crystal size does not cause objectionable unsharpness of the image. For all practical purposes, the speed of such screens may be considered constant.

Cones should be employed in every projection and be of a size that will adequately center the area of interest on the film. If cones are not available, diaphragms of suitable aperture cut from sheet lead should be inserted in the tube-head channel.

Grids should be employed wherever indicated. Because they vary in their roentgen-ray absorption characteristics, a slight adjustment in the milliampere-second values listed may perhaps be necessary to secure the most satisfactory results.

Thickness Ranges. The modern soldier conforms to a definite physical standard and may be considered a normal adult. For that reason, a group of over six hundred soldiers was studied to determine, by actual measurement, the thickness of those parts of the body traversed by the roentgen-ray beam when employing various projections. As a consequence, a series of normal thickness ranges was established. Since the *thickness* of any body part is not an index of its

TECHNIQUE CHART

For Use with U.S. Army X-ray Field Unit

Region	Average Thickness—(Adult) cm.			Basic ma-sec.		Optimum kv. (peak)	Distance
	Antero-posterior	Postero-anterior	Lateral				
Thumb Finger	1.5–4			45	F	55	
Hand	3–5						
			7–10	120	F		
Wrist			5–8				
	3–6			45	F		
Forearm	6–9			75	F	60	30″
			7–10	105	F		
Elbow	6–9						
			7–10	120	F		
Arm	7–10			5	S		
			7–10	3.75	S		
Shoulder Clavicle	12–16			15	S		
		13–17					
Foot	6–9			52.5	F		
			6–9	90	F		
Ankle			6–9			65	
	7–10			105	F		
Leg	9–12			5	S	60	
			8–11	3.75	S		
Knee	10–14			5	S	65	
			9–13	3.75	S		
Thigh	14–17			30	SG	75	
			13–16	22.5	SG		
Hip	17–21			60	SG		
Cervical vertebrae C1-7			10–13	22.5	S	85	72″
Cervical vertebrae C1-3	12–15			60	SG	65	30″
Cervical vertebrae C4-7	11–14			45	SG		
Thoracic vertebrae	20–24			60	SG	75	
			28–32			85	

Directions—

Kv. (*peak*) value is read on:

1. *No load*, when community line is stable.
2. *Load*, when community line is unstable or gas-electric generator is used.

Always align long axis of tube with that of part and direct cathode portion of roentgen-ray beam toward area of greatest tissue density.

Symbols: F = plain film; S = screens (med. speed); SG = screens and grid

TECHNIQUE CHART—*continued*

For Use with U.S. Army X-ray Field Unit

Region	Average Thickness—(Adult) cm..				Basic ma-sec.		Optimum kv. (peak)	Distance
	Antero-posterior	Postero-anterior	Lateral					
Lumbar vertebrae			27–32		150	SG	85	
	18–22							
Pelvis	20–23				90	SG	70	
Gallbladder		20–24						
Gastrointestinal tract		18–22			25	SG		
		18–21			30	SG	85	30″
			13–17		15	SG		
Skull	16–23				37.5	SG		
				Inf.-Sup. 20–25	75	SG		
Pars petrosa (Stenvers)				Post-Lat. 15–19	22.5	S	70	
Sinuses All			13–17		5.625	S	65	
Sinuses Frontal		18–21			9.375	S		
Sinuses Maxillary		18–22			18.75	S	75	
Facial bones		18–22			15	S		20″
Mandible			9–12		3.125	S	70	
Mastoid and temporomandibular articulation			14–17		7.5	S		
Chest	20–25				3.75	S		40″
Chest Small		–19			1.875	S		
Chest Average		20–25			3.75	S	80	60″
Chest Large		26–29			7.5	S		
Chest Huge		30–			15	S		
			27–32		18.75	S	85	48″
		Obl. 24–30			11.25	S		

Ma-sec. value is:

1. *Halved*, when thickness is *less* than average.
2. *Basic*, when thickness is *average.*
3. *Doubled*, when thickness is *greater* than average.
4. *Quadrupled*, if roentgenographic density is insufficient for anteroposterior pelvis or anteroposterior lumbar spine.

Note special factors for posteroanterior chests.

Roentgenographic density is gained by *ma-sec.* not *kv. (peak).*

For best results, use *time-temperature processing* with an exhaustion chart.

Compiled by: Major Arthur W. Fuchs, Sn. C.

physiology or its roentgen-ray absorptive qualities, it cannot be employed *per se* as an authoritative index of the roentgenographic density desired to be produced. Every body part consists of a proportionate amount of bone and flesh with a normal fluid content, irrespective of thickness. Experimental roentgenograms of normal adults have made possible the determination of exposure factors, particularly kilovoltage, that will yield the best quality of image. The kilovoltage selected for each projection was determined to be optimum for the part examined; the milliampere-second value selected provided the most acceptable roentgenographic density in each case—a density that is entirely translucent when viewed before a roentgen-ray illuminator. Also, the optimum kilovoltage was selected on the basis that it not only provided a wave length that would fully penetrate the part and produce a minimum of secondary radiation, but that it would provide a long scale of contrast so essential for maximum visualization of detail.

The normal thickness range need not be accurately determined in roentgenography by the experienced technician. All that is needed is a visual classification of the part as small, average or large. For the *small* part the basic milliampere-second value is haved; for the *average* part, the basic milliampere-second value is employed; and for the *large* part, the basic milliampere-second value is doubled (in a few instances, quadrupled). By means of these modifications, the roentgenographic density obtained will be approximately correct in every instance; if not, a slight increase or decrease in the milliampere-second value in exposing a second film should provide the most desirable density. However, it will be found that this procedure is seldom required.

Some deviations from the usual procedure should be made in certain classes of patients: the milliampere-second value ordinarily employed for a part should be halved in roentgenography of the aged or those debilitated by disease such as metastasis. When the average part is encased in a cast, the milliampere-second value should be doubled. If the part is large and in a cast, the milliampere-second value should be quadrupled.

A consolidated technique chart, including standard roentgenographic projections, is shown on pages 362–363. For the sake of simplicity, special techniques have been omitted. The chart was primarily developed for use with the U.S. Army X-ray Field unit which employs self-rectified current. When fully rectified apparatus is employed, the basic milliampere-second values as listed may provide slightly greater roentgenographic densities than is most desirable. If so, the desirable percentage of increase or decrease in milliampere-seconds may be easily determined by trial and added to or subtracted from the basic value. The kilovoltages need not be changed because they have been proved qualitatively optimum for the projections listed. *Any density differences should always be compensated for by milliampere-seconds and not by kilovoltage.* Calibration of apparatus should be reasonably correct in that the pre-reading kilovoltmeter should indicate the approximate kilovoltage applied to the tube. When a non-variable community line is used, kilovoltage readings may be made on *no load* with no appreciable change in roentgenographic quality. Where the line is variable—for example, when employing a gas-electric generator—readings should be made *on load.* The kilovoltages employed are few in number and are in convenient multiples of 5. Smaller multiples have no practical roentgenographic significance.

Application of Technique. From the foregoing data, it is possible to abstract certain essential facts and combine them into an exposure system which complies with the following roentgenographic requirements:

1. To provide roentgenographic images in which detail is visible throughout the entire image—bone as well as flesh detail.
2. To provide an image which is the result of full exposure; no areas of under-

or over-exposure are present in the area of interest.

3. To penetrate thoroughly the part examined by radiation which is qualitatively influenced by an optimum kilovoltage, thereby assuring a long scale of contrast with the production of a minimum of secondary radiation fog.

It is most important that the processing procedure be standardized to insure uniform results. When processing is a constant, any gross departures from normal roentgenographic densities may be attributed more particularly to pathological tissue changes. Standard time-temperature processing, employing a developer exhaustion chart,* precludes at least 50 per cent of all possible variables.

An example of the correct procedure in applying the optimum kilovoltage technique will clarify its use. Suppose that a shoulder is to be examined and an anteroposterior projection is to be employed. The first step is to determine the correct optimum kilovoltage and the basic milliampere-second value to be employed at a selected anode-film distance. Next, the part should be classified as to size—whether small, average, or large.

* These charts may be secured free of charge from the Eastman Kodak Company, Medical Division, Rochester, New York.

Reference to the chart indicates that the average thickness range is 12–16 cm.; the opimum kilovoltage is 60; the basic ma-sec. is 15; the distance is 30 inches. Medium speed screens and a cone to cover a 10×12 inch film should be employed. If the thickness of the part classifies it as *small*, 7.5 ma-sec. is used; if *average*, 15 ma-sec.; and if *large*, 30 ma-sec. The kilovoltage remains the same in each instance. The central ray is projected through the localization point, and the cathode portion of the roentgen-ray beam is directed medially toward the region of greatest tissue density.

CONCLUSION

The ideas expressed in the foregoing may seem radical upon casual examination, but they will be found upon analysis to consist of a simplification of all the theories we have held regarding roentgenographic technique. Acceptance of the principles of the optimum kilovoltage technique and the use of the technique chart will clarify any doubts concerning its efficacy.

The need is obviated for a multiplicity of kilovoltages when employing the optimum kilovoltage technique and it may be possible to simplify the construction of the modern autotransformer employed for roentgenography.

ROENTGENOGRAPHIC TECHNIQUES: SOFT TISSUE, SURFACE DETAIL, FOREIGN BODY LOCALIZATION

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INDUSTRIAL roentgenologists in general confine their attention to studies of inanimate objects. The present paper, however, presents the results of a series of experiments performed in these Laboratories in which newly developed techniques have been applied to the roentgenography of the human body. Although developed primarily for the examination of commercial products, these techniques have aroused so much discussion and so many interesting speculations as to specific medical fields in which they may prove useful, that this preliminary report seemed indicated. The roentgenograms shown were chosen for the purpose of illustrating the principles involved and not because of any clinical significance; accordingly no claims can be made that they were recorded by the use of accepted medical roentgenographic procedures. We do believe, however, that the principles herein discussed can, in the hands of a skilled roentgenologist, be of considerable value. Actually three sets of experiments are involved. The first of these concerns an immersion technique, which should prove of interest in connection with soft tissue roentgenography; the second is an approximate method for locating embedded objects, which should be helpful in the localization of foreign bodies such as shell fragments; the third is a method for revealing surface details such as finger prints and other skin markings.

In all branches of radiology, one of the ever present problems is that of increasing the relative contrast of the images produced by the various parts of the subject being roentgenographed. Most of the modern improvements in technique and equipment have led to methods for increasing specifically the contrast of some selected portion of the image. Among these may be listed such outstanding techniques as the use of the Potter-Bucky diaphragm, the laminagraph,[11] the non-screen film, barium meal, thorotrast in arteriography, CO_2 injections in fasciagraphy, and a large list of others. While attempting to study by roentgen-ray photography certain industrial products which were opaque to light, this need for added contrast was particularly acute. No combination of voltage, milliampere-time, or type of film could be found which would reveal satisfactorily the details within and on the surface of the commercial objects being studied. Accordingly with a view to developing new methods, a study of the fundamentals of roentgenography led to the belief that certain techniques of the photographer and the optical microscopist could also be employed to advantage in this field. The success of these experiments was such that further attempts were made in order to extend the usefulness of these techniques to the field of medical roentgenology with the results described below.

THEORETICAL CONSIDERATIONS

Method for Calculating the Opacity of Substances to Roentgen Radiation. Since all roentgenograms are shadow-graphs which are taken with the object between the source of radiation and the film, a discussion of the laws governing the transmission of roentgen rays through matter is of importance. It has been accepted that the relationship which holds has the form of the well known Lambert's law of optics which can be expressed by the equation:

$$I = I_0 e^{-\mu x} \qquad (1)$$

In this equation, I is the intensity of the transmitted radiation, I_0 is the intensity of the radiation incident upon the object

in question, x is the thickness of the object, and μ is the absorption coefficient of the material of which the object is composed. This latter coefficient is a function of the mean atomic number of the material in question, the specific gravity of that material, and the wave length of the roentgen radiation employed. Exactly in what manner the absorption coefficient, μ, is a function of the material and the wave length of the roentgen radiation is a matter which has been investigated by scientists for many years. It is known that the factors preventing roentgen rays from going directly through any object are (*a*) photo absorption, ∂ and (*b*) scattering σ as is expressed in equation (2).

$$\mu = \partial + \sigma \tag{2}$$

The scattering factor, σ, is so small in magnitude that it does not usually enter into the calculations in roentgenology. However, scattered radiation is sufficiently important that Potter-Bucky diaphragms are necessary for reducing the fogging on the film which it otherwise would cause in the roentgenography of thick objects. The scattering of the roentgen radiation in going from the source to the object through air is reduced somewhat when cones or filters are used. For most practical purposes the absorption coefficient can be considered primarily as a photo absorption factor ∂, i.e., a factor expressing the power of the material to convert roentgen radiation into radiation of longer wave lengths, such as visible light or heat.

When the material is composed of more than one chemical element (which is usually the case except in the roentgenography of metals), each chemical element contributes its share in the absorption in proportion to its concentration C_i as shown by the following detailed equation for the coefficient μ of equation (1):

$$\mu = \left[C_1\left(\frac{\mu}{\rho}\right)_1 + C_2\left(\frac{\mu}{\rho}\right)_2 + C_3\left(\frac{\mu}{\rho}\right)_3 \cdots \right]\rho \tag{3}$$

where $(\mu/\rho)_i$ is the mass absorption coefficient of each element, C_i is the fraction of that element present, and ρ is the density.

Numerous attempts[8] have been made to produce a very simple and useful expression of μ_i as a function of the atomic number z_i of the chemical element in question and the wave length, λ, of the roentgen radiation. Although no equation has been found which covers a sufficiently wide range of wave lengths, the equation of Bragg and Pierce[3] is given here to show qualitatively that the absorption increases very rapidly with an increase in atomic number or wave length,

$$\frac{\mu}{\rho} = CZ^4\lambda^3 \tag{4}$$

where C is a constant. Practical use of this equation is limited by the fact that the value of C changes abruptly for every chemical element at critical wave lengths, these wave lengths being known as the "absorption edges" of the element considered. However, equation (4) has gained some popularity when reduced to the form,

$$\left(\frac{\mu}{\rho}\right)_i = K_i\lambda^3 \tag{5}$$

where $K \sim CZ_i^4$. Lingley and Elliot,[12] in their excellent discussion of soft tissue roentgenography, have presented a table containing a list of various tissues of the body together with their specific gravities and their $K\lambda^3$ values as determined by Zuppinger.[13] A similar list as taken from Zuppinger's paper is shown in Table 1 because of its usefulness later in the discussion.

An Alternate Method for Calculating the Opacity of Substances. In the work at these Laboratories, however, a different procedure is followed for determining the absorption. First an estimation is made of the mean wave length of roentgen radiation from the roentgen tube at the applied kilovoltage using published graphs[2] of wave

TABLE I

ABSORPTION COEFFICIENTS OF SOME CHOSEN SUBSTANCES

Substance	Specific Gravity	Chemical Composition	Photo Absorption Coefficient
Water	1.0	H_2O	$2.506\lambda^3$
Protein	—	C 52%, H 7%, N 16%, O 24%, S 1%	$1.78\lambda^3$
Fat (human)	0.9	C 75.6%, H 12.6%, O 11.8%	$1.135\lambda^3$
Muscle (lean)	—	W 72%, E 20%, F 6.7%, Sa 1%	2.57
Blood	1.06	W 80%, E 19.1%, Sa 0.9%	2.61
Pus	1.06	W 90.6%, E 7.8%, F 0.8%, Sa 0.8%	2.67
Sinew (connective tissue)	1.1	W 62.9%, E 34.7%, F and related substances 1.9%, inorganic Sa 0.5%	2.37
Fatty tissue	0.92	W 11.7%, E 21%, F 86%, As 0.2%	1.37
Liver	1.06	W 76%, E 20%, F 3%, As 1%	2.61
Spleen	1.05	W 78%, E 16%, F 5%, As 1%	2.61
Kidney	1.06	W 83.5%, E 15.7%, As 0.8%	2.62
Thyroid gland	1.06	W 82%, E 16%	2.70
Mammary gland (old atrophied)	0.96	W 45%, E 9.7%, F 44.8%, As 0.5%	1.93
Placenta	1.06	W 85%, F 0.85%, As 0.9%, E 13.25%	2.75
Nerves	1.03	W 76%, E 7%, Ch and Lipoid 13.5%, As 1.5%	3.12
Bone cortex	1.9	W 26%, E 24.5%, F 23%, As 47.2%	13.24
Cartilage	1.11	W 72%, E 26.3%, As 1.7%	2.70
Finger nail	—	C 51%, H 6.8%, N 16.9%, O 21%, S 3%, As 1%	2.57
Rectal adenocarcinoma	1.06	W 76%, E 22.9%, As 1.1%	2.67
Chemical glassware (Jena)	ca 2.6	SiO_2 77%, K_2O 7.7%, Na_2O 5%, CaO 10.3%	15.05
Sand stone or quartz	2.3–2.9	SiO_2	10.25
Iron	7.66	Fe	107.7

W=Water, E=Protein, F=Fat, Sa=Salts, As= Ash, Ch=Cholesterin

length versus intensity at different voltages. Then the mass absorption coefficient $(\mu/\rho)_i$ of each element at that wave length is obtained from tables.[14] With these data, equation (3) is used directly. As an illustration, at 30 kv. the mean effective wave length was estimated to be .63 Å. The absorption coefficient of water for this radiation may be calculated by knowing that the mass absorption coefficient of hydrogen at this wave length is .435 and of oxygen is .90, that water is 11 per cent hydrogen and 89 per cent oxygen, and the density is unity.

$$\mu_{H_2O} = [.11 \times .435 + .89 \times .9]1 = .85.$$

TABLE II

MASS ABSORPTION COEFFICIENTS OF SOME OF THE ELEMENTS FOUND IN ORGANIC MATERIALS

Chemical Element	Symbol	$\left(\frac{\mu}{\rho}\right)$ at $\lambda = .63$ Å
Oxygen	O	.90
Hydrogen	H	.435
Carbon	C	.467
Nitrogen	N	.610

Table II shows some of the mass absorption coefficients at $\lambda = .63$ Å of elements commonly encountered in the roentgenography of organic materials, while Table III illustrates the results of the use of the data in Table II when applied in equation (3).

The compounds for Table III were so chosen as to demonstrate the influence of density and of chemical composition on the value of the absorption coefficient, μ. The first two compounds have high absorption

coefficients partly because of their high density. The remaining compounds are arranged in the order of their decreasing oxygen contents.

Criteria for Detection of Occluded Objects. For an object to cast upon a photographic film an image which can be distinguished from the background, it is necessary that the intensity of the radiation striking the film at this point be sufficiently different from that striking the neighboring points to give rise to a discernible photographic density difference. Although the photographic properties of the particular film used, as well as the techniques and chemicals employed in processing the film, are very important factors in attaining these differences in density; no discussion of these factors will be given in this paper. It is sufficient to say that by the use of reasonable care in developing the present day commercial roentgenographic film, a distinct image can be obtained if (1) the nature of the occluded object is such that there is a difference of at least about 2 per cent between the intensity striking the film at the image and that striking the immediately surrounding areas, and if (2) the applied kilovoltage is so adjusted that about 82 per cent of the roentgen rays are absorbed in going through the subject. It is, therefore, of interest to determine the theoretical requirements imposed upon an occluded object for it to cast a distinct image upon a background resulting from the material surrounding the object. Suppose the intensity, I_i, of the radiation striking the image is expressed by equation (6), while the intensity, I_b, striking the surrounding area is expressed by equation (7),

$$I_i = I_0 e^{-(\mu/\rho)_0 \rho_0 t_0} = I_0 e^{-S_0} \tag{6}$$

$$I_b = I_0 e^{-(\mu/\rho)_m \rho_m t_m} = I_0 e^{-S_m} \tag{7}$$

where $(\mu/\rho)_0$ and $(\mu/\rho)_m$ are the respective mass absorption coefficients of the object and medium, ρ_0 and ρ_m are their densities, and t_0 and t_m are their thicknesses. If the difference between I_i and I_b must be equal to or greater than 2 per cent, then

$$I_b - I_i \geqq .02 I_b \quad \text{or} \quad I_i \leqq .98 I_b \tag{8}$$

$$\frac{I_i}{I_b} = .98 = \frac{e^{-S_0}}{e^{-S_m}} = e^{-\Delta S} \tag{9}$$

from which

$$\Delta S \geqq .02. \tag{10}$$

The second requirement (which is incidentally fulfilled when one follows the instruction charts in the roentgenographic manuals in adjusting the kilovoltage for different parts of the human body depending upon the thickness) is expressed by equation (11).

$$I_b = (1 - .82) I_0 = I_0 e^{-S_m} \tag{11}$$

from which $S_m = 1.7$. Then it follows that

$$\frac{\Delta S}{S_m} = \frac{.02}{1.7} = .012 \text{ or } 1.2\% \tag{12}$$

or $S_0 - S_m \geqq .012\ S_m$.

TABLE III

ABSORPTION COEFFICIENTS OF SOME ORGANIC COMPOUNDS

Compound	% O	% H	% C	% N	Density	μ .63
Formic acid	69.6	4.35	26.2	0.0	1.22	.943
Urea	26.7	6.66	20.0	46.7	1.33	.86
Water	89.0	11.0	0.0	0.0	1.0	.85
Methyl alcohol	50.0	12.5	37.5	0.0	0.79	.54
Ethyl alcohol	34.8	13.0	52.2	0.0	0.80	.49
Propyl alcohol	26.7	13.3	60.0	0.0	0.80	.46
Butyl alcohol	21.6	13.5	64.8	0.0	0.81	.45
Cyclohexane	0.0	14.3	85.7	0.0	0.66	.31
Nujol	(a petroleum fraction)				.87	.41
Paraffin	(a petroleum precipitate)				.89	.42

Since the value of S for a material, as seen from equations (6) and (7), is the product of mass absorption coefficient (μ/ρ), the density ρ, and the thickness t of the material it follows that the visibility of an image may be affected by a predominance of any one of these three factors or by a combination of all of them. For example, in the roentgenography of a piece of metal with a blow-hole in it, the effective thicknesses t_i of the metal at different parts is the predominating factor. In this case it has been found experimentally that a bubble is visible only if its diameter exceeds about 2 per cent of the thickness of the block.[15] This means that in metallography, ΔS must exceed 2 per cent of S_m for an image to be seen, which represents a poorer accuracy than the theoretical limit of 1.2 per cent. Also, from an inspection of Table 1, one may see that if the mass absorption coefficients were the only factors involved in medical roentgenography, not only fat tissue and bone should be visible against a background caused by muscle, but most of the other body substances except blood and liver should be visible. However, most of the individual tissues and organs of the human body are so small in thickness as compared to the effective thickness of the subject and often so intertwined than they do not produce a distinct image. In other words, the thickness factor overshadows the absorption factor in the S_m values of many of the body substances, making ΔS less than the theoretical 1.2 per cent.

In general, it may be stated that, not only in metallography does the experimental sensitivity fall short of the theoretical sensitivity, but in most other fields of roentgenography numerous factors contribute to the obliteration of the image. One of these factors is the outside shape of the subject. When the thickness of the subject is a variable due to the external shape, the logic involved in equations (6) to (11) breaks down because then t_m and, therefore, S_m are variables. The resulting theoretical sensitivity, although difficult to calculate, can be prophesied intuitively and demonstrated experimentally to be poor. This factor may be greatly corrected, however, by the technique of immersion, which effectively makes the thickness, t_m, of the material a constant.

Before discussing the technique of immersion, however, it would be of further interest to demonstrate experimentally the validity of the theoretical limits of sensitivity as set forth in equation (12), i.e., $S_0 - S_m$ must exceed about 1.2 per cent of S_m for an image to be observable. To test this, a block of paraffin (Fig. 1, *A*) with the top and bottom molded plane parallel, so that equation (12) is operative, had drilled into it six holes and in the holes were placed liquids having different absorption coefficients. The thickness of the block was

TABLE IV

Compound	Thickness, t	μ	$S=\mu t$	$S_t=S_b+S_s$	$\Delta S=S_m-S_t$	$\%\Delta S=\frac{(S_m-S_t)100}{S_m}$
Paraffin background or subject	4.4 cm. $=t_m$	.42	1.85 $=S_m$			
Paraffin below hole	4.4 − .6 = 3.8 cm.	.42	1.6 $=S_b$			
1. Nujol	.6 $=t$	.41	.246, S_0	1.846	+0.004	0.0
2. N-butyl alcohol	.6	.45	.27, S_0	1.87	−0.02	−1.1
3. Methyl alcohol	.6	.54	.323, S_0	1.923	−0.073	−3.9
4. Acetic acid	.6	.696	.417, S_0	2.017	−0.167	−9.0
5. Water	.6	.85	.51, S_0	2.11	−0.26	−14.0
6. Air	.6	0	0, S_0	1.6	+0.25	+13.0

4.4 cm. and the depth of each hole was 0.6 cm. Figure 1, *B* shows the roentgenogram obtained, while Figure 1, *C* indicates the location of the holes, their liquid contents and the percentage change in $S_m - S_0$ due to the liquids. Table IV shows the protively the limitations postulated by equation (12).

In Table IV S_m is the absorption exponent of the paraffin block when no holes are drilled, S_b is the absorption due to paraffin above and below the holes, S_0 is

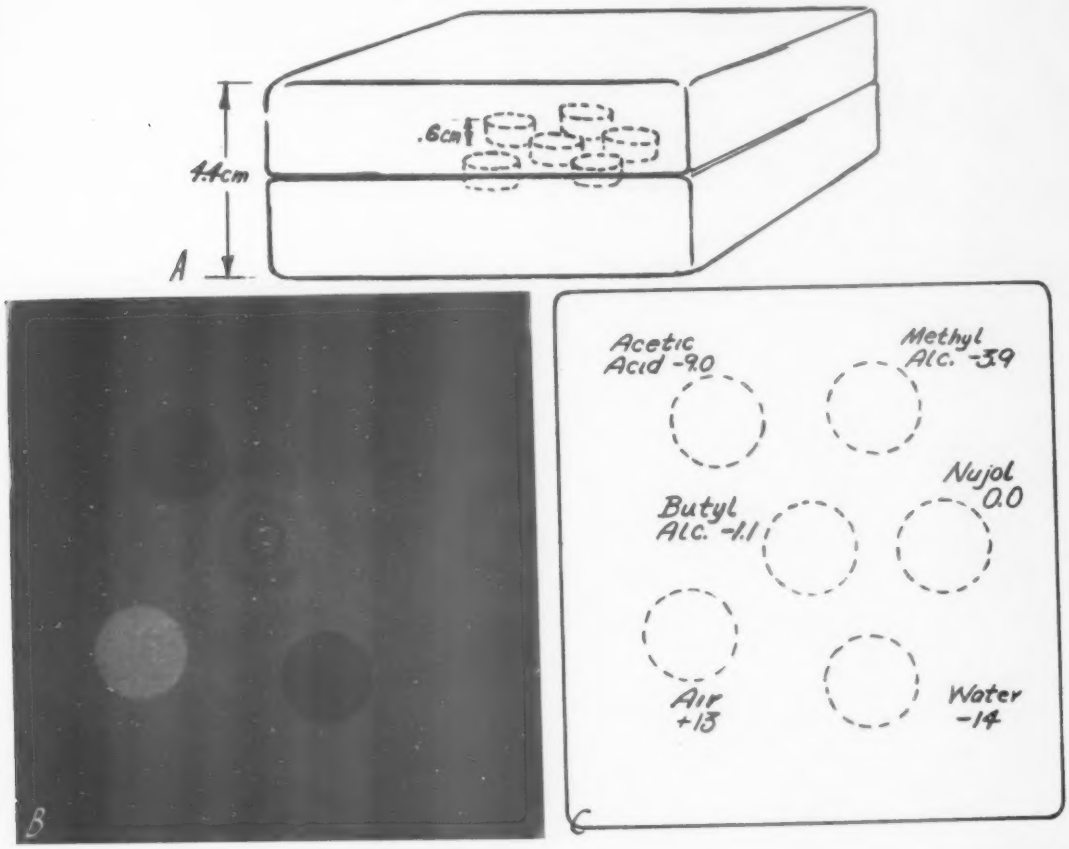

FIG. 1. *A*, paraffin block showing the arrangement of holes drilled in the top. *B*, roentgenogram of the paraffin block while *C* indicates the location of the liquids and percentage change in *S* produced by their presence. Note that nujol and normal butyl alcohol produce no image, while methyl alcohol casts a faint image and that the image of the air hole is opposite in shade to the remainder.

cedure by which the latter values were obtained. It may be observed that nujol which is almost the same in opacity as the paraffin and normal butyl alcohol whose ΔS value is only 1.1 per cent cast no measurable images, while methyl alcohol ($\Delta S = -3.9$) produces a very faint image, and acetic acid and water produce strong images. The experiment verifies qualitathe absorption due to the content of the holes, and S_t is the total absorption due to all matter in the path of the roentgen radiation, i.e., the upper paraffin block, the filled hole, and finally through the 0.6 cm. paraffin base.

IMMERSION TECHNIQUE

In usual practice, roentgenograms are

FIG. 2. Hand roentgenographed in usual manner.

taken with the objects surrounded by air. Immersion in liquids of selected opacities appears to be of importance, particularly if the chosen opacity exactly equals that of the external part or the continuous phase of the heterogeneous object being

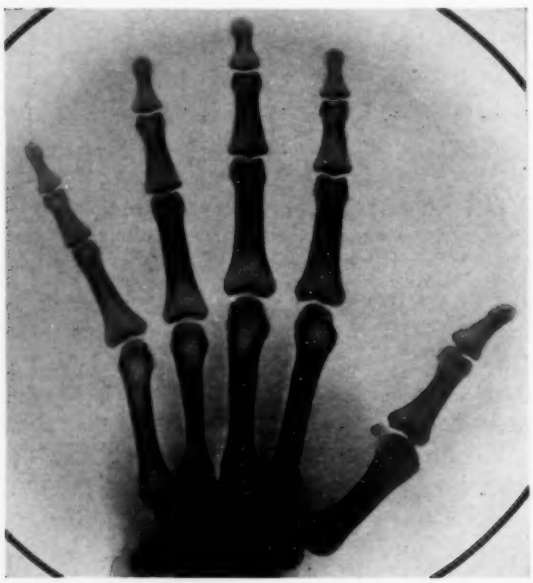

FIG. 3. Hand in water. Due to the size of the container used, the water did not cover the wrist.

FIG. 4. Hand immersed in nujol. Since nujol is not as opaque to roentgen radiation as is flesh, the contours of the flesh are visible.

studied. This choice is analogous to the choice of a suitable mounting medium for objects to be studied under the optical microscope. In the latter case, the medium is chosen to have optimum refractive index

FIG. 5. Hand immersed in a solution of 7 per cent barium chloride in water. Since this solution is more opaque than flesh, the roentgen rays have penetrated the hand more than the solution.

to give rise to the desired degree of contrast. If this refractive index can be made to match that of only one component of the object in question, that component can be made to disappear entirely. On the other hand, if this index is chosen to be as different as possible from that of the object being studied, the resulting contrast is greatly increased.

Figure 2 shows a hand roentgenographed in air, while Figure 3 shows the same hand immersed in water. As may be expected from an inspection of the absorption co-

Fig. 6. Roentgenogram of a hand dipped in a slurry of barium sulfate in nujol and the excess rubbed off. Note the effect of the external shape produced by this application.

efficients of water and flesh in Table I, the contrasts due to the contours of the flesh have become sufficiently reduced in Figure 3 so that only the bone structure is prominent. This is not surprising in view of the fact that flesh is very largely composed of water; however, due to the measurable difference in their absorption coefficients (Table I) the outlines of the fingers are faintly discernible. In complete accord with the above discussion the fleshy parts of the hand shown in Figure 4 did not vanish. In this case nujol was substituted for

Fig. 7. Roentgenogram of an arm, a portion of which was coated with an opaque paste to produce the effect of roundness. It is noted that the outer edges of the fatty layer have become more clearly defined.

water as the immersion liquid. As may be seen in Table III, nujol is less opaque to roentgen radiation than water and, therefore, should not reduce the flesh images as markedly. By choosing a liquid (7 per

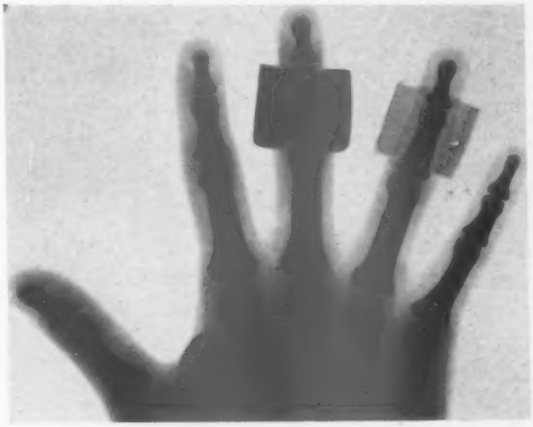

Fig. 8. A portion of the hand roentgenographed in air but having the second finger embedded in a paste having an opacity much greater than flesh. The third finger is embedded in a wax whose opacity nearly matches flesh.

cent $BaCl_2$ in water) considerably more opaque than flesh, the image of the flesh (Fig. 5) becomes much lighter than the background and the roentgenogram tends to give added emphasis to the image of the flesh. In this case one is, in effect, recording a hole the shape of the hand in the opaque immersion liquid. Although Figures 3 and 4 are shown for illustrative purposes, it is believed that the immersion liquids which will have the greatest use in medical roentgenography will be those whose opacities equal that of the outside phase of the part being studied. While water is a reasonably good immersion liquid for a muscular appendage such as a hand, an immersion liquid whose opacity is intermediate between that of water and nujol might be required if, for example, the object were heavily embedded in fat, whose opacity is lower than muscle (see Table 1).

It may at times prove helpful in interpreting a roentgenogram if the outlines of the part under study were shown on the film. This may be accomplished by spreading a film of opaque material on the surface of the part in question. A thin slurry of finely divided barium sulfate in nujol suffices for this purpose. Figure 6 illustrates such an application on the human hand and Figure 7 shows the application on an arm.

In order to avoid the practical difficulties which might arise in applying liquid immersion, the part being roentgenographed may be packed in a paste or jelly of suitable consistency and the upper and lower surfaces of this cast made parallel. Figure 8 shows a hand in air in which two fingers have been packed in this manner. The pastes used have respectively the same opacities as water and a 7 per cent solution

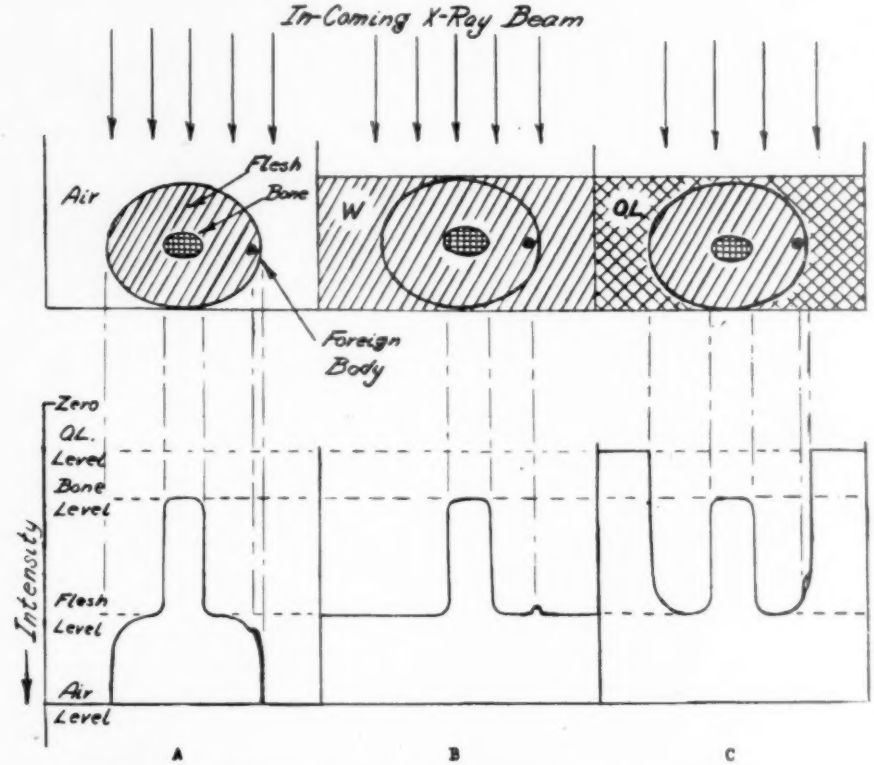

FIG. 9. Density levelling effect of immersion technique. Intensities of transmitted radiation are plotted downward as ordinates in lower half of diagram. In *B*, opacity of immersion liquid equals that of flesh. Note levelling effect. *A*, sketch of finger roentgenographed in air; *B*, same in water; *C*, same in opaque liquid (O.L.). Note in *B*, image of foreign body falls on field of uniform density.

of barium chloride in water. Starting with a radiolucent paste such as results from mixing 100 parts of petrolatum with 50 parts of beeswax any desired opacity can be obtained by blending in measured quantities of a very finely divided inorganic compound such as barium sulfate or zinc oxide.

The elimination, by immersion, of the effect of thickness differences caused by the gross shape of the part being studied has already proved its merits in more than one clinical case. For example, following an accident a hand was thought to contain glass fragments. An ordinary roentgenogram in air revealed the presence of several large pieces. A water immersion roentgenogram showed very clearly, in addition, several small glass fragments.

The explanation of the greater visibility of images from the inclusions in an immersed specimen lies in the fact, stated in the theoretical section, that slight photographic density differences are seen most clearly when they occur against a uniform background. This density leveling effect is shown schematically in Figure 9.

It is worth while to state that the immersion technique does not interfere, but rather adds to the desirable effects attained by other techniques. For instance, the injection of radiolucent gases and of radiopaque colloidal dispersions such as skiodan or thorotrast[4,5,6,9,10] has proved itself to be of great value for increasing the visibility of the images of many selected parts of the human body. The benefits of these injections would be enhanced when coupled with immersion. In fact, immersion alone might in certain cases produce sufficient visibility of the image without recourse to the more delicate injection methods.

Fig. 10. Hand coated over the palm with an opaque paste, consisting of litharge and nujol mixed to a creamy consistency.

Fig. 11. Hand coated over the posterior surface with an opaque paste.

Localization of Foreign Bodies

As described above, the immersion of a hand in a liquid whose opacity exactly matches that of flesh causes the contrast in image due to a foreign body to be more pronounced. In many cases, in addition to merely proving the existence of a foreign body it is equally desirable to find its exact location. This may be accomplished by a combination of the two methods, surface coatings and triangulation, as described below.

If instead of immersing the hand, or in addition to immersing the hand, the lower surface is coated with a suitable opaque film, a perfect two-dimensional map of the

FIG. 12. Example of the use of triangulation to determine position of objects in the hand. A double exposure has been made, the roentgen tube having been shifted at right angles to the metal wire which is on the upper surface of the hand. The relative displacements of the images of this wire and those of any embedded object allow calculations of the depth of these objects.

hand is obtained. Upon this map, the bones plus the opaque bodies are clearly located. Similarly, the top surface only of the hand may be revealed in all its detail. Figures 10 and 11 show these effects clearly.

Once it became clear that the upper and lower skin surfaces could be superimposed upon the opaque bone structures, the problem of determining three-dimensionally the position and orientation of an embedded opaque object was undertaken. A method, even if only approximate, was desired whereby the required information could be recorded on a photographic plate in a minimum of time. A procedure has been developed which involves the least possible manipulation and calculation. A single roentgenogram is obtained which allows immediate visualization of the depth and orientation of the foreign body with respect both to the skin surface and any bones in the vicinity. In contrast to methods depending upon roentgenoscopy, this procedure yields a photograph, containing internal and external reference marks, which may be used during the course of any subsequent operation. In most cases the speed and simplicity of this method should more than compensate for any lack of utmost precision. For the speedy location and removal of shell fragments, for example, where the least amount of handling of the patient and the minimum of equipment are required, this very simple method should prove desirable.

An opaque mark is placed on the upper and lower skin surfaces in the vicinity of the suspected foreign object. A series of two roentgen-ray exposures are taken upon the same film, the roentgen tube being moved laterally between exposures. The lower mark, since it is very close to the roentgen film, causes a single image while the upper opaque mark gives two images of equal intensity. All other opaque objects give rise to double images whose linear separations are approximately proportional to the height of the object above the lower mark. By single triangulation it can be shown that the distance, x, of an embedded object

FIG. 13. An example of the combined use of double exposure and surface coating for the possible location of foreign bodies. The palm is coated with yellow lead paste and one wire is on the posterior surface of the hand.

from the lower surface is given immediately by the equation:

$$x = \frac{T \cdot d}{D} \qquad (13)$$

where T is the calipered (in place) thickness of the section roentgenographed or the height of the upper skin mark above the photographic plate, d is the linear displacement of the image of the foreign object, and D is the displacement of the image of the upper reference mark. (If the distance x is subtracted from T, the expression $T-x$ gives the distance of the object from the upper skin surface.) Convenient marks may be obtained by applying short lengths of metal wire to the skin by means of scotch tape. Figure 12 shows this simple technique as applied to the hand.

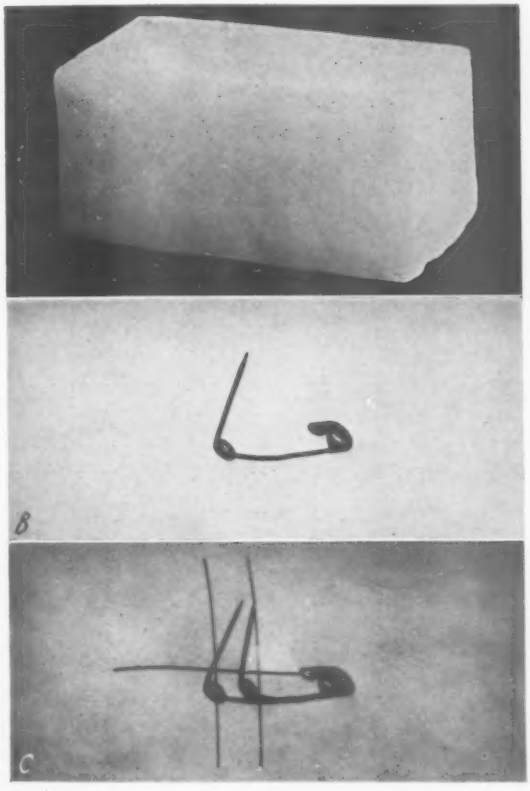

Fig. 14. *A*, ordinary photograph of a block of paraffin wax known to contain a safety pin. *B*, a single exposure roentgenogram of a safety pin in the block of paraffin. From this it cannot be determined whether the point is up or down. *C*, a double exposure roentgenogram of the pin in the block of paraffin. In this roentgenogram it is seen that the point is toward the film while the loop is away from the film.

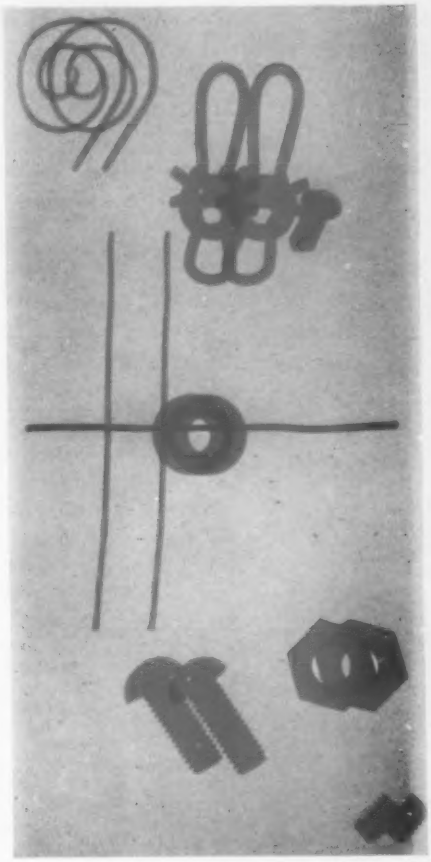

Fig. 15. A double exposure roentgenogram of a paraffin block which contained a number of pieces of metal embedded at different depths. It was from this roentgenogram that data for Table 11 were obtained.

If instead of the lower wire, the surface nearer the roentgen film is coated as in Figure 13 a two-dimensional map is also recorded.

In the absence of clinical cases and for purposes of illustration, an open safety pin was hidden in a block of paraffin, and given to the roentgenologist as an unknown. As presented in Figure 14, *A*, *B* and *C*, it is easy to visualize or to measure in three dimensions the orientation of the object.

As a check upon the precision and speed of this method, several foreign objects were

embedded in a block of paraffin. The roentgenogram in Figure 15 was taken and the measured values of $T=6.0$ cm. and $D=0.81$ cm. were substituted in equation (13), obtaining the equation

$$x=\frac{T\cdot d}{D}=\frac{6.0d}{.81}=7.42d \qquad (14)$$

Within a few minutes after developing the plate, the calculated values of x (column III, Table V) were obtained. The block was then cross-sectioned and the values in column IV were found by measurement. A comparison of these values shows clearly that the accuracy of this simple method is sufficient for most purposes.

TABLE V

ILLUSTRATING THE USE OF TRIANGULATION FOR LOCATING THE HEIGHT OF OBJECTS ABOVE THE FILM

I Object	II Shift d	III Calculated height, x	IV Measured height, x	V Error
Spiral	0.45 cm.	3.4 cm.	3.3 cm.	0.1 cm.
Toggle head, top	0.78	5.8	5.9	0.1
Toggle head, bottom	0.54	4.0	4.0	0.0
Small screw, head	0.04	0.3	0.2	0.1
Small screw, point	0.12	0.9	0.8	0.1
Washer	0.25	1.8	1.8	0.0
Bolt head	0.68	5.0	5.0	0.0
Bolt end	0.68	5.0	5.0	0.0
Hexagonal nut	0.37	2.8	2.9	0.1
Set screw	0.40	3.0	3.0	0.0

A survey of the literature shows that many methods for the use of triangulation have been suggested and used for the localization of foreign bodies. Some of these make use of auxiliary equipment, others involve very exact and time-consuming calculations, while still others employ roentgenoscopy which yields no photographic record. A very good discussion of some of these methods may be found in Section 27 of Clark's excellent volume.[7]

In Table V the calculated heights were obtained by use of equation (14) in the text.

Among journal articles discussing special techniques in soft tissue roentgenography, one by Allen and Calder[1] is of interest. In certain cases a combination of this triangulation method with the technique of immersion may be of practical value.

ROENTGEN-RAY FINGER PRINTS AND HAND PRINTS

If the anterior surface of the hand is coated very carefully with an opaque paste as described above, it is possible to record finger prints and hand prints of excellent character. The authors are indebted to Mr. E. F. Champaygne of these Laboratories for the following discussion and the roentgenograms pertaining thereto.

If the lower surface of the hand and fingers are coated uniformly with a litharge paste and roentgenographed while only a layer of black paper separates the hand and the film, the picture shown in Figure 10 is obtained. In this picture the finger prints are visible through the bone, and immediately suggests the use of roentgen rays in recording finger prints for the records of the police and government bureaus. One of the chief merits of this method is the procurement of the skin detail of the entire hand accompanied by a record of the bone detail. Although it may never be possible to formulate a system for bone structure classification as effective in its use as that used for finger prints, there are certainly

enough identifying features on the bones of a given hand to allow that hand to be selected from a limited few which might be suspected. The ability to make such a selection on the basis of bone structure might be extremely important if the finger prints had been destroyed accidentally by fire or acid or intentionally with the object of escaping identification.

In full accord with the theories of roentgenography, the recording of finger prints through the bone is made possible by certain conditions quite opposite to those conditions most favorable to soft tissue study. The first of these conditions is the use of a high kilovoltage (50–70 kv.) on the roentgen tube, thus generating roentgen radiation of short wave length and therefore so penetrating that the flesh of the hand absorbs only a small fraction of the radiation, and the bone absorbs by no means all of it. Under these conditions the bulk of the burden of stopping the radiation falls upon the palm and finger coatings which, because of the furrows and ridges of the flesh, are extremely variable in thickness. To obtain the maximum contrast, litharge (lead oxide) was chosen as the coating material, being previously brought to the consistency of ordinary facial cream by stirring into the litharge trial quantities of nujol. The resulting paste is coated on the hand to a thickness which appears to permit the ridges of the flesh to protrude.

Fig. 16. An enlarged roentgenogram showing the fineness of detail made possible by the use of a litharge coating and high kilovoltage.

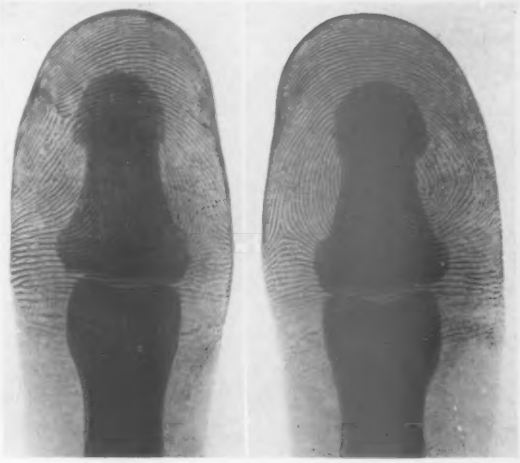

Fig. 17. An enlarged roentgenogram of two thumbs. Note the detail in the scar on the left thumb, and the imperfect branching of the furrows in the center.

To demonstrate fully the fineness of detail obtainable by this method an enlargement is shown in Figure 16 of the second finger of the left hand and in Figure 17 the thumb of each hand. It is believed that the information recorded in these roentgenograms exceeds that obtainable from the ordinary finger print.

CONCLUSION

As implied in the introduction, these techniques were developed for accomplishing various tasks in connection with the application of roentgenology to a series of commercial problems. This presentation is

made in the sincere hope that they may also yield to successful application in the field of medical roentgenology.

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METABOLIC CHANGES OCCURRING AS THE RESULT OF DEEP ROENTGEN THERAPY*†

I. THE EFFECT OF 200 KILOVOLT ROENTGEN THERAPY

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THIS investigation was undertaken with the idea of determining what changes in the body economy result from deep roentgen therapy, especially in relation to the symptom complex known as "irradiation sickness" and in relation to the wave length of radiation. The investigation was restricted in scope to certain aspects of nitrogen and inorganic salt metabolism. Considerable work has already been done on this problem, but the most striking feature of reports of previous workers is their divergent conclusions. These variations are possibly explained by unstandardized roentgen-ray dosage and, in the case of metabolism studies, by the use of diets of unknown chemical content. The reviews of Rolleston[27] and Warren[33] serve to demonstrate this point very well, and an excellent summary of the literature is to be found in a more recent article by Graham.[14]

The determination of the basal metabolic rate has shown no consistent change in man or animals[8,12,21] following irradiation.

Total nitrogen excretion has been studied by numerous investigators.[2,8,9,10,11,15,22,25,34] Most of these found increase in nitrogen excretion of greater or lesser degree, varying with the intensity and duration of irradiation, area of the body exposed, and type of lesion treated.

Uric acid was the first fraction of the total nitrogen excretion to receive special attention. Most authors[5,6,8,11,18] found increased excretion of uric acid and interpreted this as evidence of increased purine excretion consequent upon nuclear disintegration. An interesting paper[4] cites instances of ureteral obstruction by uric acid masses following radiation therapy.

The acidity of the blood and acid-base balance have been the subject of much investigation.[10,13,25,35] The only conclusion that can be drawn from the literature is that no significant change in pH occurs as a result of exposure to roentgen rays.

Chloride excretion and blood chloride levels have been frequently studied.[7,8,9,17,24,29] Increased and decreased elimination and blood levels have been found, but lack of adequate control of intake diminishes the importance of much of the earlier work. Several references to beneficial effect of sodium chloride ingestion in roentgen sickness were noted.[7,24,29]

Increased phosphorus excretion is a fairly regular finding after irradiation and has been practically always interpreted as the result of protoplasmic, probably nuclear, destruction.[8,9,10,11,26,32]

Calcium metabolism[1,31] and carbohydrate metabolism[14,33] have generally been found to show no important or consistent changes as a result of exposure to roentgen rays.

METHODS

The patients observed in this study were on constant, accurately weighed diets, potentially neutral, low in purines and calcium, and in most instances minimal in chloride. A special research dietitian had charge of the diets and devoted all of her time to at most two patients. All refused food was weighed and intake figures calculated only for food actually eaten. These

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† This is Reprint No. 576 of the Cancer Commission of Harvard University.
‡ Now Clinical Director of Longview Hospital, Cincinnati, Ohio.

TABLE I

Patient	Age	Sex	Diagnosis	Diet	Irradiation					Roentgen Sickness		Clinical Effects of Treatment
					Area treated and size of field	Filter	Time	Daily dose (r)	Total (r)	Nausea*	Vomiting	
A No. 30-893	55	F	Carcinoma of left breast	High chloride	Left breast and chest 20×20 cm.	0.5 mm. Cu, 4 mm. Al	2 hr. 36 min.	170	680	++	None	Slight decrease in size of axillary lymph nodes
B No. 30-1468	20	M	Malignant lymphoma	High chloride	Neck 20×20 cm.	0.5 mm. Cu, 4 mm. Al	2 hr. 36 min.	160	320	0	None	Large gland in neck almost completely disappeared
C No. 30-1316	49	F	Atypical lymphoblastoma	Low chloride	Spleen and liver 20×20 cm.	0.5 mm. Cu, 4 mm. Al	2 hr. 36 min.	170	680	0	None	Decrease in size of liver and spleen; inguinal nodes smaller
D No. 30-1594	22	F	Osteochondrosarcoma of pelvis	Moderate chloride	Pelvis 20×20 cm.	0.5 mm. Cu, 4 mm. Al	2 hr. 36 min.	170 plus 4000 mc-hr. radium	680 plus 12,000 mc-hr. radium	++	None	No effect upon size of tumor
E No. 31-282	50	F	Adenocarcinoma, probably of bronchial origin, metastatic to cervical and axillary lymph nodes	Low chloride	Chest 20×20 cm.	0.5 mm. Cu, 4 mm. Al	1 hr. 15 min.	400	1600	+++	None	Slight increase in the mediastinal mass following treatments
F No. 31-350	66	F	Malignant lymphoma	Low chloride	Neck and face 20×20 cm.	0.5 mm. Cu, 4 mm. Al	1 hr. 15 min.	400	1600	+++	Second day of treatment	Masses in right parotid, right temporal and left submaxillary regions practically disappeared
G No. 31-1162	56	F	Recurrent carcinoma of right breast	Very low chloride	Chest 20×20 cm.	0.5 mm. Cu, 4 mm. Al	35 min.	400	1200	+++	On second and third days and two days following treatment	Lesion somewhat smaller in size and less troublesome

TABLE I (*Continued*)

Patient	Age	Sex	Diagnosis	Diet	Irradiation					Roentgen Sickness		Clinical Effects of Treatment
					Area treated and size of field	Filter	Time	Daily dose (r)	Total (r)	Nausea*	Vomiting	
H No. 30-360	55	F	Carcinoma of cervix	Low chloride	Pelvis 20×20 cm.	0.5 mm. Cu	30 min.	300	2400	+	On sixth day of treatment	Some relief from pain but no appreciable change in size of tumor mass
I No. 31-318	58	F	Adenocarcinoma of uterus with metastases in lungs	Moderate chloride	Chest and abdomen 20×20 cm.	0.5 mm. Cu	25 min.	300	2300	o	None	Marked regression in lesion of lung
J No. 31-1427	26	M	Malignant lymphoma	Moderate chloride	Right neck 10×10 cm.	0.5 mm. Cu	30 min	300	600	o	None	Mass in neck disappeared fairly rapidly
K No. 32-4	62	F	Carcinoma of right breast	Very low chloride	Right breast 20×20 cm.	0.5 mm. Cu	30 min.	300	1200	+++	On first, third and fourth days of treatment and on day following	No effect upon size of tumor
L No. 32-452	56	F	Recurrent carcinoma of right breast with metastases in lymph nodes	Very low chloride	Right breast 20×20 cm.	0.5 mm. Cu	30 min.	300	1200	+	On day following treatment	Some relief from pain

* o=no ill effect; +=slight nausea, no refusal of food; ++=nausea, slight refusal of food; +++=severe nausea, refusal of food.

figures were taken from Sherman's tables[30] supplemented by analyses of inorganic constituents made in this laboratory. Chloride was determined on actual aliquots of the total daily diets, since the chloride content of individual foodstuffs had previously been found to vary markedly in different samples.[28] As far as possible, foodstuffs low in chloride were chosen, supplemented by weighed amounts of sodium chloride.

The careful metabolic routine employed has been reported elsewhere[3]. The time of observation was divided into continuous periods of two days each and carmine and charcoal were given alternately to separate the feces. Analyses of urine, feces, and vomitus, if any, were made for inorganic constituents, the loss in vomitus being added to the fecal excretion figures in the tables. Nitrogen, uric acid, and other components of the nitrogen partition were determined on the urine only. The mass of these data is so great that, unfortunately, publication in full is not possible. Some of the more striking temporary changes, especially in the first periods after irradiation, are not made obvious in the summarizing tables but these are discussed in the text. Routine urine examinations and blood analyses in these patients disclosed no renal defects to distort the metabolic results.

The analytical methods used for titratable acidity, phosphorus, sulphur, and calcium were those of Henderson and Palmer, Fiske and Subbarow, Fiske, and Fiske and Logan, respectively. Chloride determinations were made on the blood by Van Slyke and Sendroy's open Carius method; on the urine by Volhard's method; on the feces by the open Carius with Volhard titration. The nitrogen constituents were analyzed by the methods of Folin. These methods are all available in textbooks (Folin, Hawk and Bergeim, Peters and Van Slyke).

Irradiation was carried out on successive days until the total dose indicated in each case was given. Dosage was measured in air (Table 1). The treatments lasted two to eight days at the discretion of the radiologist. The treatment on each day usually lasted not more than one hour. In the first 4 patients studied, lower voltage radiation was used and the exposure was longer. The dosage of radiation was less than in the more recent cases, but definite therapeutic effect was obtained.

The radiation apparatus was entirely separated from the patients. The roentgen tubes were enclosed in a large lead-lined chamber with portals for exposure of the patients. These portals were closed off with filters for the rays and the chamber ventilated by a fan. The control box, rectifiers, transformers, etc., were on the floor below. Noxious gases and loud machinery can therefore be left out of consideration as causes for the changes studied in this investigation.

RESULTS

The level of the basal metabolism was not found to vary significantly in 8 cases studied.

In 11 patients pH and carbon dioxide, and in 4 of these patients oxygen determinations were also made on arterial blood as part of an investigation by Lund.[20] In no case did he find any significant change following irradiation, either immediately or at varying periods thereafter.

PROTEIN METABOLISM

Changes in the excretion of total nitrogen and its components are the most definite deviations from the control values presented by these investigations (Table 11). There is, in general, an increase in the urinary output of total nitrogen either during the periods when radiation was being given or in those which immediately followed cessation of treatment. Of the 12 patients studied only 2 (K and L) failed to show this increase. In several patients who refused part or most of their food following irradiation, the increase in nitrogen excretion is more apparent in the negative nitrogen balance. In such patients it is

TABLE II

NITROGEN METABOLISM

Patient	Number of Periods	Total Nitrogen		Uric Acid-Nitrogen		Urinary Total Acid Excretion			Creatinine N	Amino acid N	Non-protein Nitrogen of Blood
		Urinary excretion	Balance	Urinary excretion	Ratio to total N	Titratable acidity minus CO_2	Ammonia	Titratable acidity plus ammonia	Urinary excretion	Urinary excretion	
		grams	grams	grams		cc. N/10	cc. N/10	cc. N/10	grams	grams	mg. per 100 cc.
A											
Before	2	14.2	2.9	0.24	1.7						31
Roentgen Irradiation	3	14.4	1.5	0.30	2.1						31
After	2	16.8	−0.1	0.30	1.8						29
B											
Before	2	16.0	2.1	0.33	2.1						18
Roentgen Irradiation	1	21.0	−3.1	0.47	2.3						
After	3	15.3	3.4	0.48	2.7						22
C											
Before	2	16.8	1.4	0.36	2.2	251	623	874			38
Roentgen Irradiation	2	18.1	0.0	0.51	2.8	401	615	1016			32
After	4	18.9	−1.0	0.47	2.6	444	628	1072			31
D											
Before	3	17.1	2.8	0.44	2.3	316	615	931			28
Roentgen Irradiation	2	18.5	−2.0	0.53	2.9	381	573	954			20
After	4	20.1	−0.7	0.49	2.7	290	737	1027			25
E											
Before	4	24.5	3.0	0.47	1.9	567	637	1204			22
Roentgen Irradiation	2	25.5	−2.0	0.56	2.2	600	630	1230			27
After	8	23.3	1.0	0.52	2.2	376	813	1189			20
F											
Before	5	22.4	0.1	0.41	1.8						18
Roentgen Irradiation	2	19.5	−5.4	0.62	3.2						27
After	3	17.9	−6.8	0.41	2.3						22
G											
Before	5	11.1	0.9	0.30	2.7	224	320	544			18
Roentgen Irradiation	2	13.3	−5.7	0.43	3.2	335	412	747			20
After	9	11.6	−1.1	0.31	2.6	284	344	628			18
H											
Before	2	13.6	0.2	0.31	2.3	311	565	876	0.75	0.14	24
Roentgen Irradiation	4	14.5	−3.4	0.37	2.5	308	628	936	0.76	0.13	22
After	1	14.1	−5.4	0.40	2.9	294	581	875	0.70	0.12	
I											
Before	5	14.7	−2.4	0.29	1.9	365	478	643	0.58	0.13	32
Roentgen Irradiation	4	16.9	−4.3	0.38	2.2	463	675	1138	0.55	0.13	29
After	4	17.3	−5.2	0.34	2.1	352	642	994	0.58	0.11	32
J											
Before	3	22.1	−5.8	0.51	2.3	364	636	1000	1.38	0.20	28
Roentgen Irradiation	1	24.8	−8.1	0.67	2.7	333	594	927	1.47	0.27	28
After	8	20.7	−3.6	0.55	2.7	362	604	968	1.36	0.13	29
K											
Before	2	12.9	−0.3	0.28	2.2	239	315	554	0.72	0.15	24
Roentgen Irradiation	2	12.5	−0.3	0.33	2.6	276	380	656	0.68	0.14	24
After	8	12.3	0.0	0.27	2.2	190	317	507	0.63	0.10	25
L											
Before	2	17.6	−3.5	0.42	2.4	649	570	1219	0.89	0.16	36
Roentgen Irradiation	2	16.9	−2.8	0.39	2.3	623	691	1314	0.84	0.13	26
After	4	17.4	−3.2	0.37	2.2	545	667	1212	0.81	0.14	24

The figures for excretion in each case represent the average per period of the number of periods given in column 2.

TABLE III

INORGANIC SALT METABOLISM

Patient	No. of Periods	Calcium			Phosphorus			Chloride			Serum Values		
		Excretion		Balance	Excretion		Balance	Excretion		Balance	Ca	P	Cl
		Urinary	Fecal		Urinary	Fecal		Urinary	Fecal		mg. per 100 cc.	mg. per 100 cc.	m. eq. per liter
		gm.	gm.	gm.	gm.	gm.	gm.	gm.	gm.	gm.			
A													
Before	2	0.25	0.17	−0.21	0.63	0.27	0.29				10.9	4.3	
Roentgen Irradiation	3	0.24	0.24	−0.27	0.69	0.36	−0.01				8.9	4.6	
After	2	0.25	0.40	−0.45	0.74	0.41	−0.05				—	—	
B													
Before	2				0.82	0.44	0.17					3.3	
Roentgen Irradiation	1				1.10	0.22	0.11					4.0	
After	3				0.81	0.24	0.37					3.6	
C													
Before	2	0.14	1.04	−0.24	1.19	0.56	0.01				10.0	3.6	
Roentgen Irradiation	2	0.12	1.02	−0.20	1.27	0.61	−0.12				10.0	4.4	
After	4	0.12	0.94	−0.15	1.28	0.60	−0.12				10.0	4.0	
D													
Before	3	0.33	0.27	−0.37	0.85	0.41	0.08	4.67		·0.05*	10.3	3.6	96
Roentgen Irradiation	2	0.38	0.24	−0.41	1.09	0.60	−0.59	5.34		−1.22*	10.2	4.0	96
After	4	0.42	0.32	−0.52	1.10	0.55	−0.30	5.57		−0.86*	9.8	4.2	97
E													
Before	4	0.11	0.26	−0.14	1.10	0.62	0.34	1.89	0.18	0.43	10.4	4.6	104
Roentgen Irradiation	2	0.14	0.27	−0.20	1.12	0.57	−0.09	2.36	0.12	−0.20	9.6	4.2	100
After	8	0.12	0.24	−0.15	0.90	0.52	0.33	1.62	0.14	1.11	9.6	4.9	100
F													
Before	5	0.13	0.19	−0.11	1.02	0.46	0.00	2.66	0.33	−0.87	9.6		102
Roentgen Irradiation	2	0.13	0.11	−0.12	1.24	0.22	−0.63	2.30	0.26	−1.49	8.9		100
After	3	0.14	0.23	−0.16	0.94	0.33	−0.55	1.79	0.41	1.00	—		99
G													
Before	5	0.23	0.30	−0.22	0.65	0.42	0.09	2.48	0.22	−0.22	9.6	3.4	102
Roentgen Irradiation	2	0.30	0.22	−0.36	1.02	0.30	−0.67	2.77	0.19	−2.36	9.5	3.3	99
After	9	0.24	0.21	−0.16	0.65	0.35	−0.03	1.02	0.12	0.63	9.8	3.2	103
H													
Before	2				0.76	0.41	−0.11	1.69	0.34	0.15		3.8	105
Roentgen Irradiation	4				0.85	0.34	−0.31	1.18	0.36	0.15		3.6	107
After	1				0.88	0.33	−0.53	1.19	0.77	−0.46		—	—
I													
Before	5	0.19	0.32	−0.32	0.88	0.35	−0.27	2.49	0.23	0.65	9.2	4.0	104
Roentgen Irradiation	4	0.16	0.35	−0.33	1.26	0.42	−0.72	2.46	0.08	0.83	9.4	3.9	103
After	4	0.11	0.39	−0.32	0.93	0.47	−0.43	2.63	0.16	0.58	9.3	3.2	105
J													
Before	3				0.96	0.29	−0.27	2.41	0.14	0.53			103
Roentgen Irradiation	1				1.40	0.48	−0.36	2.90	0.04	0.18			99
After	8				1.44	0.57	−0.48	2.17	0.15	0.79			102
K													
Before	2				0.58	0.19	0.08	1.73	0.07	0.17		3.7	107
Roentgen Irradiation	2				0.70	0.36	−0.22	1.51	0.12	−0.14		3.9	104
After	8				0.62	0.37	−0.15	0.86	0.05	0.72		—	104
L													
Before	2	0.22	0.25	−0.23	1.16	0.55	−0.46	1.28	0.32	−0.11	8.4	3.4	107
Roentgen Irradiation	2	0.25	0.24	−0.23	1.23	0.53	−0.50	0.76	0.32	0.35	9.9	3.5	105
After	4	0.23	0.32	−0.29	1.13	0.62	−0.50	0.57	0.56	0.35		3.5	106

The figures for excretion in each case represent the average per period of the number of periods given in column 2.

* Not including fecal excretion

difficult to evaluate changes of this sort because breakdown of body protein could be attributed to starvation as well as to irradiation. The amount and duration of the nitrogen loss varies from patient to patient, but it is definitely greater in patients with radiosensitive tumors, as indicated by disappearance of the mass following treatment (B, F, I and J).

In several patients more complete nitrogen partition studies were made. Both uric acid and, to a lesser degree, ammonia were found to be involved in this nitrogen increase. The endogenous uric acid excretion was found to be increased in all cases but one (L), and in this case the excretion shown in the individual analyses was too variable to be of any signifiicance when averaged. What is perhaps more important than the increased excretion is that the ratio uric acid nitrogen: total nitrogen was increased. Even in those cases with small actual increases in uric acid excretion, this ratio is definitely elevated as may be seen in Table II.

Although the variations in ammonia and titratable acidity were not large, the total acid of the urine was definitely higher in most cases during or after roentgen therapy. This increase might be attributed to voluntary starvation in roentgen sickness except that it was not limited to patients showing symptoms of intoxication. It may, however, be evidence of greater destruction of body protein with consequent increase in urinary excretion of acid radicles. Such an increase is actually demonstrated in the phosphate elimination of most of these patients, as may be seen in Table III.

In 5 patients creatinine and amino acid were also studied. No significant change can be said to have taken place in the excretion of these nitrogen fractions as a result of irradiation. It is interesting, however, to note that in all 5 patients a slight diminution in amino-acid nitrogen excretion took place two to six days after irradiation and continued to the end of the observations. In the patients whose study continued for several periods after treatment, the total nitrogen balance also seemed to indicate storage of nitrogen after the primary destructive effect of irradiation had worn off. This is more striking in the detailed data than in the average balances shown in our tables.

The nonprotein nitrogen of the blood was found to vary during roentgen therapy from the control values but the results were not consistent. Following irradiation blood uric acids in patients A, G, H, J and K showed significant increase at one or more observations (0.5 mg. per 100 cc. or more).

INORGANIC SALT EXCHANGE

In 8 of the 12 patients studied, complete analyses of calcium excretion were made (Table III). No significant deviation of the calcium balance from control values was found. In one case (G) there was a slight increase in urinary excretion during one of the two day periods of roentgen therapy. As this patient refused practically all food during this time, the increased negative balance was to be expected. Serum calcium was found to vary only within normal limits (10 ± 1 mg. per 100 cc. serum). No connection was seen between either serum calcium or calcium balance and roentgen sickness.

Determination of the phosphorus excretion and balance was made in all 12 patients (Table III). The most common variation was an increase in the urinary phosphorus output during or following roentgen therapy with deviation of the balance to the negative side. As others have also indicated, the increase in phosphorus output during a period of lowered phosphorus intake is most likely the result of destruction of protoplasmic structure. That nuclear material very probably is profoundly affected is indicated by the simultaneous increase in uric acid and phosphorus excretion. The inorganic phosphorus of the blood in most cases remained constant.

Total sulfur of urine and feces and sulfate of urine were determined on combined periods of several patients and on separate periods in one. A small but definite increase

in the urinary sulfur and sulfate occurred following irradiation. The fecal sulfur excretion was not constantly or consistently affected.

The chloride metabolism studies present several interesting and suggestive features which may best be brought out by grouping the subjects according to their chloride intakes. Two of the patients (A and B) were given as much as 4 to 5 gm. of chloride per day, 3 (D, I and J) a more moderate amount, while the remaining 7 were given a diet containing a minimal amount of chloride (1.25 gm. or less a day). Four of the patients in this last group (E, F, G and K) ,who had been given a low chloride diet for several days preceding the study periods, showed characteristic symptoms of severe roentgen intoxication following treatment. The remaining 3 were on the diet for only six days before irradiation. One of these (C) who received relatively mild treatment had no symptoms; the other 2 suffered moderate anorexia, but one (L) ate all the food offered her; the other (H) was so dissatisfied that the study was terminated early. Of the 4 severely stricken patients only one (K) was able by sheer force of determination and persuasion to consume the same diet that she had eaten in the control period. Of the 5 patients on moderate or high chloride intake 2 became ill (A and D). Their symptoms were of shorter duration, however, than those of the patients in the low chloride group and their food intake was reduced slightly in each case for only one day. It seems, therefore, that a long period of chloride starvation preceding irradiation may be considered a definite factor in predisposing to irradiation sickness, even though in some instances sickness may supervene without this factor. Furthermore, as previous workers have noted, sodium chloride by mouth is very frequently an effective therapeutic agent in irradiation sickness. We administered this salt in doses of 3 to 5 gm., usually in ginger ale, to several patients with anorexia following roentgen treatments, including 2 of the patients in this study (E and F). In some cases its action was dramatic. Patient E demanded beef steak for supper within a few hours after receiving 3 gm. of sodium chloride. Other patients responded more slowly, but very few seemed not to benefit. These findings are similar to those of Neuda, Redlich and Sielmann,[24] and those of Schlagintweit and Sielmann.[29]

The most interesting facts in the study of the chloride metabolism, however, are found in the balance studies (Table III). All of the patients who became severely ill (D, E, F, G and K) showed a definite chloride loss during the irradiation period, as shown by the negative balances even though in some cases less salt was ingested, and 2 of these patients (F and G) had shown consistently negative balances before irradiation, also. In every one of these 5 patients the chloride balance became positive shortly before or simultaneously with improvement in symptoms. Patients E and F received some sodium chloride by mouth, patients D, G and K received nothing in the way of treatment. The added chloride in patients E and F was taken up as by a sponge and did not reappear in the excreta during the study period. It is also interesting to note that those patients who were without evidence of roentgen sickness maintained a consistently positive chloride balance indicating more or less storage of chloride.

The blood of most of these patients showed a lowered chloride value approximating the renal threshold level. In no case, however, was the decrease very striking.

DISCUSSION

In accord with some other investigators roentgen irradiation has been shown by these studies to cause abnormalities in the nitrogen and chloride metabolism of man.

The significance of the increase in nitrogen excretion which was found in almost every case was partially clarified. That the increased nitrogen loss is influenced by tissue destruction seems apparent from

those cases in which large tumor masses melted away following treatment. But cases in which no gross destruction took place also showed definite increases in nitrogen excretion even after discounting the effect of anorexia and consequent refusal of food. All the cases which were studied long enough after irradiation showed a period of nitrogen storage following the period of nitrogen loss.

There is no characteristic increase in amino-acid excretion accompanying the negative nitrogen balance at the beginning of radiation therapy but a significant diminution of amino-acid excretion accompanies nitrogen storage following irradiation. Very likely the amino acids formed in the early period of destructive roentgen-ray effect are partly metabolized to other end products for excretion. On the other hand, when tissues are being regenerated, amino acids are retained for tissue regeneration.

The localization of the destructive effect of irradiation at least to some degree is indicated by further study of the nitrogen partitions. The increase of the endogenous uric acid excretion may be considered evidence of increased purine metabolism from destruction of nuclear material. What part of the increased phosphorus excretion also comes from such a source cannot be calculated from the data, but a certain proportion very likely has its origin in broken down nuclei. The variability of the increase of uric acid excretion may result as much from differences in ability to metabolize purines as from differences in irradiation effects.

The increases in phosphorus and sulfur excretion are also probably traceable to the destruction of protein by roentgen rays. In most patients the balances of phosphorus and sulfur run practically parallel.

The fluctuations of the chloride exchange call for some comment. No other substance showed a similar correlation to roentgen intoxication. The outstanding points to be noted are: (1) the susceptibility to roentgen sickness of patients with protracted sodium chloride starvation; (2) the greater chloride loss synchronous with symptoms of roentgen sickness, even on minimal intakes of sodium chloride; (3) the storage of chloride when the symptoms of illness abated, so that chloride excretion was reduced in some cases almost below measurable levels; (4) the favorable response of some patients to the administration of sodium chloride in roentgen intoxication. Such deviations immediately bring to mind the changes in sodium chloride exchange found originally by Loeb[19] and by Harrop and his co-workers[16] in adrenal cortical deficiency. Our patients, however, show no accompanying blood concentration; that is, no variation in hematocrit values or nitrogen retention such as they found; but therapeutic doses of roentgen rays can hardly be expected to produce such drastic changes as are found in animals or men deprived of all or most of the adrenal cortex, or was as found in irradiated dogs by Moon, Kornblum and Morgan.[23]

Previous authors have dealt only with normal or elevated chloride intakes. High chloride intakes tend to make the excretion of chlorides more variable than minimal intakes because of the power of the organism to store chloride with and without water so that the effect of other factors upon the chloride exchange might be masked in consequence. It is probable that the patients who were on minimal chloride intake indicate more nearly the changes actually occurring in the body cells and fluids. Sudden and marked retention, such as was found by Cori and Pucher,[8] and Cameron and McMillan,[7] was not seen in this series.

Direct damage of abdominal organs by irradiation cannot be considered the cause of roentgen intoxication since several of the patients who were irradiated over the abdomen showed little or no evidence of intoxication while those who did suffer as the result of irradiation were irradiated in widely separated areas: 4 receiving treat-

ment over the chest, one over the neck and parotid gland, and one over the posterior and lateral aspects of the pelvis.

All consideration of psychogenic causes for irradiation sickness are excluded from this discussion because accurate evaluation of the mental factor is not possible. Besides, the finding of a suggestive chemical change associated with such sickenss reduces the relative importance of mental factors.

CONCLUSIONS

(1) Cases were subjected to careful prolonged study of nitrogen and inorganic salt metabolism before, during and after irradiation.

(2) The nitrogen partition studies show some increase during the periods of roentgen therapy, in the total, and the uric acid nitrogen excretions as well as in the total acidity of the urine, followed by retention of amino-acid nitrogen after irradiation was stopped.

(3) These results, as well as increase in phosphorus and sulfur excretion, are probably attributable to protein breakdown following roentgen-ray exposure.

(4) Chloride studies suggest a definite relation between chloride metabolism and roentgen sickness.

(5) Creatinine and calcium excretion were unaffected by roentgen treatment.

(6) No specific changes result from roentgen-ray exposure in every patient. These conclusions are simply the summarizing of trends which seem apparent from the data on hand.

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METABOLIC CHANGES OCCURRING AS THE RESULT OF DEEP ROENTGEN THERAPY*

II. THE EFFECT OF 1,000 KILOVOLT ROENTGEN THERAPY

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THE development of a generator capable of producing a constant potential of 1 million volts, and the successful designing of a roentgen tube to operate at that potential has made available a source of roentgen rays of short wave length and high intensity. The possibility that these differences in quality of the rays might result in a difference in metabolic changes induced in the human subject was suggested by the fact that irradiation sickness appeared to be definitely less frequent in patients treated with the 1,000 kilovolt roentgen rays. This study was planned to include only the least controversial elements of previous studies, as reported in the literature and as revealed in a previous study conducted in these laboratories by Goldman[9] with 200 kilovolt roentgen rays.

The earlier literature has been adequately summarized by Goldman. Beneficial effects of vitamin B and of the barbiturates in the treatment of irradiation sickness have been reported by several investigators.[10,12,13,14] There has been very little interest in the metabolic aspect of the problem in recent years and consequently few contributions have appeared. Brogsitter and Schmidt-Ott[3] studied 3 cases of leukemia on absolutely minimal nitrogen intakes (1.1 to 1.4 grams per day). They found a rise in uric acid output as well as total nitrogen. On the basis of Pocya's figures for purine content of myelogenous leukemic spleens, they calculated that 491 grams of splenic tissue had been destroyed as a result of roentgen therapy. Granatowicz[11] found a rise in the protein content of thoracic duct lymph which appeared within the first hour followng irradiation. This points to a prompt change in blood vessel permeability or lymph node destruction as a result of irradiation.

To summarize the whole literature, it can be said that with very few exceptions all workers on this problem have found an increase in total nitrogen excretion and in that of uric acid. Chloride metabolism studies have given various results, in the experience of several workers, both increased and diminished excretion having been quite clearly demonstrated.

METHODS

Patients were placed on constant, accurately weighed, neutral diets, low in purines and calcium. Sodium chloride was restricted in 4 cases, while the other 3 patients were given moderately high chloride intake. A research dietitian was responsible for the preparation of the food, which was done with the meticulous quantitative technique previously reported.[1] Previous studies in this laboratory had shown that individual foodstuffs often varied considerably in their chloride content. In this study, therefore, particular pains were taken to purchase large enough amounts of foods to last throughout the period of study of each patient. The "salt-free" canned foods which are now available were found especially helpful. An aliquot of the total daily diet was subjected to wet digestion by nitric acid in the presence of excess silver nitrate and the extract analyzed for chloride. The figures so obtained were used in compiling the data in Table III. Other dietary figures were calculated from Sherman's tables,[16] augmented with data from previous studies in this laboratory.

* This and the previous paper were presented before the Third International Cancer Congress, Atlantic City, N. J., May, 1939.
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The chemical determinations were made according to the routine methods described in Folin's Manual.[8] Nitrogen was determined by Folin's colorimetric method on blood and by Kjeldahl distillation on urine; chloride by Volhard's and Whitehorn's methods respectively for urine and serum. Uric acid in urine was determined by a slightly modified early Folin method, described in the fourth edition, rather than by the micro method given in the fifth edition of his laboratory manual. Fecal analyses were not made.

The time of observation was divided into consecutive periods of two days each and for the purposes of tabulation the periods before, during and after radiation therapy were grouped together. The analytical data in the tables represent the average per period of the number of periods in each group.

Patients were placed on the desired diet four to eight days prior to the administration of radiation. Once begun, radiation was given every day with the exception of Sundays, until therapy was completed. This varied from as few as four treatments in one case to as many as sixteen in another. The dosages in most of the patients were of the same general magnitude as were given to the patients studied by Goldman. One patient (F) received a much larger dose, however, than any of his patients received. The most striking difference was in the time factor, an adequate dose for one day being delivered in four to six minutes by the 1,000 kv. machine. Dosage was measured in air.

The influence of fright or other emotion on the part of the patient was eliminated as well as possible. The treatment room was attractively furnished, with only the target end of the roentgen tube extending through the ceiling from the floor above and directed at an adjustable table upon which the patient reclined. The entire portion of the roentgen tube within the treatment room was heavily encased with lead. The voltage generating apparatus and the controls were on the floor above, but the patient could be in instant communication with the operator through a public address system. By this arrangement the effect of loud machinery was reduced to a minimum, and the possibility of influence by gases made extremely remote by a forced draft ventilating system.

NITROGEN METABOLISM

Changes in the nitrogen metabolism, though not dramatic, are the most striking of those followed in this investigation. From Table I it may be seen that, in general, there is a shift in the total nitrogen balance toward the negative side during irradiation followed by a return to a more positive balance after the cessation of treatments. The sharpness and magnitude of these changes is, of course, less apparent in this table where only averages are shown but it is more obvious in the data of individual analyses. This diminished nitrogen balance tends to be delayed for forty-eight hours after the beginning of roentgen treatments. Interestingly enough, actual retention of nitrogen occurred in this first forty-eight hour period in 3 of the patients who continued to eat their full diet (B, C, and F).

The most striking correlation was found between the degree of nitrogen loss and the sensitivity of the patients' lesions to irradiation. In 2 patients (A and B) of the 7 studied during treatment with 1,000 kv., no increase in nitrogen excretion even in individual periods was evident during or following treatment. Both of these patients had very small amounts of carcinoma tissue (one after removal of breast, one with disease of the cervix). The 4 patients (C, D, E and G), who showed the most marked loss of nitrogen, all had Hodgkin's granuloma, which is relatively sensitive to roentgen rays. At the dosage levels employed in our patients, the site of radiation appeared to exert no influence on the nitrogen metabolism, the sensitivity of the pathological tissue to irradiation being much more significant (Table II).

In 5 patients uric acid nitrogen and in 6

TABLE I

NITROGEN METABOLISM

Patient	Number of Periods	Total Nitrogen			Uric Acid N		Creatinine N	Creatine N	Blood Values		Serum
		Urinary excretion gm.	Intake gm.	Balance* gm.	Urinary excretion gm.	Ratio uric acid N/total N	Urinary excretion gm.	Urinary excretion gm.	Non-protein nitrogen mg. per 100 cc.	Uric acid mg. per 100 cc.	Uric acid mg. per 100 cc.
A											
Before x-ray	5	19.2	19.3	0.1			1.94	0.61	19.0		
Early x-ray	5	19.3	19.2	−0.1			1.85	0.74	21.5		
Late x-ray	4	19.0	19.2	0.2			1.80	0.56	20.5		
After x-ray	3	13.1†	19.2†	6.1†			1.61	0.33	22.0		
B											
Before x-ray	4	14.4	15.8	1.4			2.17	0.60	19.0		
Early x-ray	4	13.0	15.8	2.8			2.08	0.53	20.0		
Late x-ray	4	13.1	15.7	2.6			2.03	0.37	17.0		
After x-ray	3	12.2	15.7	3.5			1.99	0.32	17.7		
C											
Before x-ray	3	19.7	18.5	−1.2	0.625	3.2	2.71	0.37	23.0	2.3	3.0
Early x-ray	1	18.1	18.6	0.5	0.614	3.4	2.70	0.04	20.0	—	—
Late x-ray	2	21.8	18.6	−3.2	0.737	3.4	3.00	0.18	18.0	2.1	3.0
After x-ray	3	18.2	18.6	0.4	0.643	3.5	2.72	0.22	17.5	2.8	3.8
D											
Before x-ray	2	14.5	15.2	0.7	0.336	2.3	2.39	0.03	15.0	2.8	4.2
Early x-ray	1	13.1	11.3	−1.8	0.348	2.7	2.23	0.13	15.0	2.8	4.5
Late x-ray	2	13.4	10.4	−3.0	0.412	3.1	2.11	0.21	—	2.3	3.7
After x-ray	3	15.2	15.2	0.0	0.312	2.0	1.98	0.51	19.0	3.0	4.3
E											
Before x-ray	2	19.2	19.3	0.1	0.509	2.6	2.46	0.11	18.0	4.8	7.2
Early x-ray	1	21.0	19.3	−1.7	0.626	3.0	2.12	0.84	—	4.4	6.4
Late x-ray	1	16.0	1.0	−15.0	0.506	3.2	2.23	0.21	26.0	6.2	8.6
After x-ray	4	19.8	15.6	−4.2	0.607	3.1	2.43	0.15	18.5	3.7	5.6
F											
Before x-ray	3	20.1	17.8	−2.3	0.484	2.4			20.3	3.8	6.0
Early x-ray	2	17.6	17.7	0.1	0.579	3.3			18.3	3.2	5.0
Late x-ray	7	19.4	17.7	−1.7	0.575	3.0			19.3	—	—
After x-ray	4	18.3	17.7	−0.6	0.444	2.4			16.6	3.7	5.8
G											
Before x-ray	4	21.5	19.1	−2.4	0.477	2.2	3.15	0.05	18.0	3.4	5.1
Early x-ray	1	21.4	19.1	−2.3	0.604	2.8	3.03	0.28	23.0	2.2	4.0
Late x-ray	2	24.2	19.1	−5.1	0.557	2.3	3.13	0.43	—	2.3	3.0
After x-ray	4	20.9	19.2	−1.7	0.533	2.5	2.75	0.38	22.0	3.0	4.5

The figures for excretion in each case represent the average per period of the number of periods given in column 2.
* Does not include loss of nitrogen through fecal excretion.
† Intake doubtful because patient uncooperative during this period.

patients creatine and creatinine nitrogen excretion were studied. There was a definite elevation in the level of urinary uric acid which fell quite promptly toward the control level after irradiation was stopped. Creatine and creatinine metabolism showed no consistent changes. The 3 male patients with Hodgkin's disease showed significant amounts of creatine in the urine, which is unusual for males.

CHLORIDE METABOLISM

The chloride metabolism studies fall into two groups on the basis of the intake level. Four patients (A, B, F and G) received minimal amounts of chloride, whereas 3

TABLE II

SUMMARY OF CASE HISTORIES

Patient	Diagnosis	Area Irradiated	Irradiation		Nausea	Vomiting
			Per field	Total		
			r	r		
A. H.H. 38-170 (M.R.) F. Age 44	Carcinoma of cervix	Pelvis, 3 fields	$5\times400\ ^{10}/_{10}$	6,000	+++	On day following treatments
B. H.H. 38-112 (M.L.) F. Age 30	Carcinoma of breast (postoperative)	Pelvis, 2 fields; right breast, supraclavicular area	$2\times300\ ^{15}/_{15}$ $4\times400\ ^{15}/_{15}$ $4\times400\ ^{15}/_{15}$	4,400	+	o
C. H.H. 38-479 (T.D.) M. Age 38	Hodgkin's granuloma	Anterior mediastinum, right groin, right axilla	$3\times200\ ^{15}/_{15}$ $4\times150\ ^{12}/_{12}$ $4\times150\ ^{12}/_{12}$	1,800	o	o
D. H.H. 38-589 (E.U.) F. Age 22	Hodgkin's granuloma	Anterior mediastinum	$1\times200\ ^{15}/_{15}$ $1\times300\ ^{10}/_{15}$ $4\times400\ ^{10}/_{15}$	2,100	++	o
E. H.H. 37-1168 (C.S.) M. Age 33	Hodgkin's granuloma	Left posterior lumbar area	$2\times100\ ^{30}/_{30}$ $3\times\ 60\ ^{30}/_{30}$	380	+++	Last two days and day following treatments
F. H.H. 38-1659 (T.B.) F. Age 47	Carcinoma of breast recurrent	Right supraclavicular area, pelvis, 2 fields	$9\times400\ ^{15}/_{15}$ $3\times300\ ^{15}/_{15}$	5,400	o	o
G. H.H. 38-1510 (W.H.) M. Age 35	Hodgkin's granuloma	Right and left axillae	$6\times300\ ^{15}/_{15}$	3,600	+	o

others (C, D and E) were given liberal allowances. Both groups received approximately the same diet of low chloride content but those on a high chloride intake (2.5 to 5 grams per day) were given in addition weighed portions of C.P. sodium chloride. The excess above the palatability of the food was administered in gelatin capsules.

As in shown in Table III both increased and diminished urinary chloride excretion was found to occur in patients studied during roentgen therapy. Two of the patients (A and B) on a minimal chloride intake (less than 1.4 grams per day) showed a gradual rise in the chloride excretion, which appeared immediately after irradiation was begun, rose to a peak within the first six days of treatment, and gradually fell off despite continued irradiation. After irradiation was stopped the chloride excretion fell more rapidly. Patients F and G, who were on an even lower chloride intake, showed a diminished output of chloride in the urine during the irradiation periods. One patient (C), a male with Hodgkin's disease, on a very liberal chloride intake, also showed a diminution of urinary chloride excretion in the treatment period. Another patient (D) on the same diet had a high urinary excretion and a negative chloride balance before irradiation was begun. After the first treatment period a diminished urinary chloride excretion

TABLE III

CHLORIDE METABOLISM

Patient	Number of Periods	Urinary Excretion gm.	Intake gm.	Balance* gm.	Serum Values m.eq./liter
A					
Before x-ray	5	2.96	2.31	−0.65	110
Early x-ray	5	3.42	2.31	−1.11	104
Late x-ray	4	3.17	2.31	−0.86	107
After x-ray	3	2.01†	2.31†	0.30†	107
B					
Before x-ray	4	1.35	2.65	1.30	110
Early x-ray	4	2.37	2.65	0.28	104
Late x-ray	4	1.93	2.65	0.72	103
After x-ray	3	1.93	2.65	0.72	110
C					
Before x-ray	3	10.3	10.6	0.3	100
Early x-ray	1	8.9	10.6	1.7	—
Late x-ray	2	9.3	10.6	1.3	101
After x-ray	3	9.7	10.6	0.9	101
D					
Before x-ray	2	11.5	10.2	−1.3	106
Early x-ray	1	11.1	9.6	−1.5	101
Late x-ray	2	10.4	9.7	−0.7	101
After x-ray	3	10.4	10.9	0.5	103
E					
Before x-ray	2	4.6	6.1	1.5	99
Early x-ray	1	6.4	6.1	−0.3	99
Late x-ray	1	3.2	1.9	−1.3	99
After x-ray	4	5.9	5.4	−0.5	99
F					
Before x-ray	3	1.16	1.42	0.26	99
Early x-ray	2	0.94	1.42	0.48	101
Late x-ray	7	0.80	1.42	0.62	100
After x-ray	7	0.86	1.42	0.56	102
G					
Before x-ray	4	1.81	1.38	−0.43	99
Early x-ray	1	0.83	1.38	0.55	97
Late x-ray	2	1.17	1.38	0.21	—
After x-ray	4	0.97	1.38	0.41	99

The figures for excretion in each case represent the average per period of the number of periods given in column 2.
* Does not include loss of chloride through fecal excretion.
† Intake doubtful, patient uncooperative in this period.

resulted in a gradual shift in the chloride balance to the positive side. The third patient (E) on high chloride intake showed an increase in chloride excretion starting as soon as irradiation was begun. In his case, chloride excretion fell promptly after irradiation was stopped only to rise seventy-two hours after the discontinuance of treatment. The serum chloride levels of all the patients remained at all times within the range of normal variations.

Three 3 patients who showed consider-

able roentgen sickness (A, D and E) were the three who also showed negative chloride balances, regardless of the chloride intake. In the 2 instances in which nausea and vomiting occurred, the time relation to changes in chloride metabolism was difficult to interpret. In one instance the vomiting occurred after treatment was stopped and the chloride loss was diminishing (Patient A); in the second instance the patient (E) was on a liberal chloride intake, but irradiation caused a slight chloride loss in the urine even before vomiting intervened to increase the chloride loss. The remaining patients showed approximately the same degree of anorexia whether their salt intake was high or low.

On the basis of these results it appears that the disturbance in chloride metabolism cannot be prevented in susceptible patients by raising the chloride intake of the food. This suggests that chloride is not primarily concerned in the initiation of roentgen sickness, but is rather linked to roentgen sickness secondarily through some as yet obscure disturbance of water balance.

One patient (E) because of a history of irradiation sickness during previous courses of treatment was given intramuscular vitamin B_1 daily throughout the period of study. This therapy, reported by Martin and Moursund[12] as beneficial, was ineffective in preventing severe irradiation sickness in this case.

In 2 patients (F and G), grouped urine periods before treatment, during treatment and after treatment, were extracted for porphyrins according to the method of Dobriner,[5] which provides for the elimination of other pigments from the porphyrin extracts before quantitating the color, as has been discussed by Dobriner and Rhoads.[6] The quantitative estimation of porphyrin was made with the Evelyn photoelectric colorimeter using the "520" filter. No increase in urinary porphyrin (coproporphyrin) occurred with treatment. This result is in essential agreement with Graham's results in that he failed to find any direct relation of degree of sickness and response to nicotinic acid therapy to porphyrin excretion. It is not in agreement with the report of Spies, Bean and Stone[17] of abnormal porphyrinuria in 7 cases of irradiation sickness.

DISCUSSION

This is the first study of metabolic effects resulting from 1,000 kv. roentgen therapy. The results have been similar to the results of the previous study conducted in these laboratories on the effect of 200 kv. roentgen therapy and are in accord with other investigations reported in the literature. Supervoltage roentgen radiation has been shown to produce an increased excretion of nitrogen, uric acid, and chloride in some of the patients, just as does lower voltage radiation.

That the negative nitrogen balance results entirely from tissue destruction is strongly indicated by its restriction to cases in which large tumor masses disappear under the influence of roentgen irradiation. In both groups of cases the magnitude of the change in nitrogen balance appeared to be roughly proportional to the rapidity with which such masses disappeared. In all cases in which study was sufficiently prolonged, a period of nitrogen storage followed that of nitrogen loss. This is not obvious in the tables because they represent averages and hence include the period of high excretion following roentgen irradiation which hides the later values which indicate retention. That food refusal and vomiting are confusing factors in such a study is evident in the exaggeration of the negative nitrogen balance, unaccompanied by increase in absolute excretion values in the affected patients.

The increased uric acid excretion may be considered to be of exactly the same significance as the nitrogen excretion values indicating the localized destruction of nuclear material.

The modifications in chloride metabolism, however, are not adequately explained by tissue destruction alone. That severe chloride deprivation is an adequate

cause in itself for anorexia, nausea and vomiting is well established. That the metabolic changes initiated by roentgen irradiation may be such as would tend to produce such a deprivation is confirmed, though it is not clear which factor initiates the cycle in roentgen sickness.

In comparing the results of this study with those of the previous study conducted by Goldman[9] in this laboratory using lower voltage roentgen radiation, certain features are worthy of mention.

The chloride changes were in agreement in the two studies in that a negative chloride balance was shown to occur, though not invariably. The occasional occurrence of positive chloride balance, as reported by Cori and Pucher[4] and Dodds and Webster,[7] has been verified in one case and points to individual variations in the fluid shifts initiated by roentgen irradiation.

The chloride changes of the negative balance type occurred less frequently in the patients treated with 1,000 kv., and roentgen sickness was observed much less frequently than it had been in the group of patients treated with lower voltage roentgen rays. This lesser frequency of roentgen sickness made it possible for more of the patients to maintain constant intakes throughout the period of study. This is in accord with our clinical impression that irradiation sickness is less frequent and less severe under 1 million volt roentgen therapy than under 200,000 volt roentgen therapy. That the changes in chloride metabolism in those cases where it did occur are not due to the greater absorption of the lower potential roentgen radiation in the superficial tissues is suggested by the fact that one of the 1,000 kv. patients who received very large doses, so that the skin was blistered and ulcerated, showed no shift in chloride balance. The effects on the total nitrogen and uric acid metabolism of irradiation with 200 and 1,000 kv. indicate a similarity in the effects of the two intensities of roentgen rays, and also shows the correlation of radiosensitivity of the irradiated lesion with degree of change in nitrogen balance.

SUMMARY AND CONCLUSIONS

(1) Seven patients were subjected to a careful study of nitrogen and chloride metabolism before, during and after 1,000 kilovolt roentgen therapy.

(2) The nitrogen studies show an increase in total and uric acid nitrogen excretion resulting from roentgen irradiation, followed by a period of retention or diminished excretion after cessation of treatments.

(3) These changes are attributable to tissue protein and nuclear tissue destruction respectively, and are roughly proportional to the rapidity of tumor disappearance after irradiation.

(4) Chloride metabolism changes in the nature of a negative chloride balance were demonstrated, but less frequently in the patients receiving the 1,000 than the 200 kv. therapy.

(5) Though this chloride change seems to be correlated with the degree of nausea and vomiting, this study suggests that it is a secondary result of a disturbance in water balance rather than the precipitating cause of the roentgen sickness.

(6) No significant differences in changes in metabolism induced by irradiation with 200 kv. and 1,000 kv. roentgen rays were demonstrated.

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RADIUM DOSAGE FOR LINEAR SOURCES*

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CALCULATION of radium dosage for filtered linear sources presents considerable difficulty for several reasons. Absorption in the radium element itself, the effect of oblique filtration, the problem of determining absorption coefficients, both for metals and tissue, the extremely steep variation in dosage near the surface of the source, and the complications introduced by end effects, all contribute to the difficulty. In addition, in tissue, the heterogeneity of the medium introduces an unknown factor.

Nevertheless, because of the frequent use of linear sources, calculations of approximate dosage from such sources are required. Calculations of this kind have been made by Sievert,[8,9] Laurence,[1,2] Quimby,[5,6] and others.[3] Data, calculated from Sievert, were included by Paterson and Parker[4] in their charts.

Unfortunately, the contributions, particularly of Sievert and Laurence, have not achieved the wide usage that they deserve. This is probably due to the fact that both of these authors presented their data in rather complicated mathematical forms.

The graphical representation of Sievert's data by Paterson and Parker is also limited in its usefulness because it furnishes an average dose, up to a distance of only 3 cm., in terms of milligram-hours for 1,000 gamma roentgens, and frequently requires interpolation.

The most uncertain factors in calculations of this sort are probably absorption and scattering in tissue. As pointed out by several authors, for a thickness up to about 3 cm., the effect of tissue may be considered unimportant in the sense of Paterson and Parker—i.e., the error introduced by neglecting it will not exceed 10 per cent. For greater distances, this ceases to be true, and unfortunately, when linear sources are used, e.g., in a uterine tandem, these larger distances are involved. The uncertainty in the calculations of tissue effects is clearly indicated when such calculations are made independently from the data of Sievert and of Laurence and compared. They are found to differ considerably, the difference increasing with increasing thickness of tissue. When linear sources are arranged in some geometrical pattern, absorption and scattering in tissue are further complicated, and the "effective" absorption coefficient varies with the particular pattern. From the small amount of data available, it would appear that this "effective" absorption coefficient may be taken without excessive error as about 3 per cent per centimeter thickness of "soft" tissue. Since the entire correction due to the effect of soft tissue is in most cases small in itself, the error introduced by using this rather arbitrary value cannot be of great importance. Therefore, because tissue absorption is small and at present cannot be calculated accurately, it would seem satisfactory to take the value for tissue absorption as 3 per cent per centimeter thickness of soft tissue and to use this value in correcting the dosage calculated without consideration of tissue effects. The data presented in this paper are therefore in the form of dosage "in air" and must be corrected to include tissue absorption when indicated.

Data from Sievert's tables may be presented in a rather simple graphical manner when values are plotted on double logarithmic graph paper. Figure 1 is such a graph for linear sources filtered by 0.5 mm. Pt or its equivalent, and Figure 2 for sources filtered by 1.0 mm. Pt or its equivalent. In order to understand how these graphs are used, a short explanation is necessary.

To convert Sievert's unit into gamma

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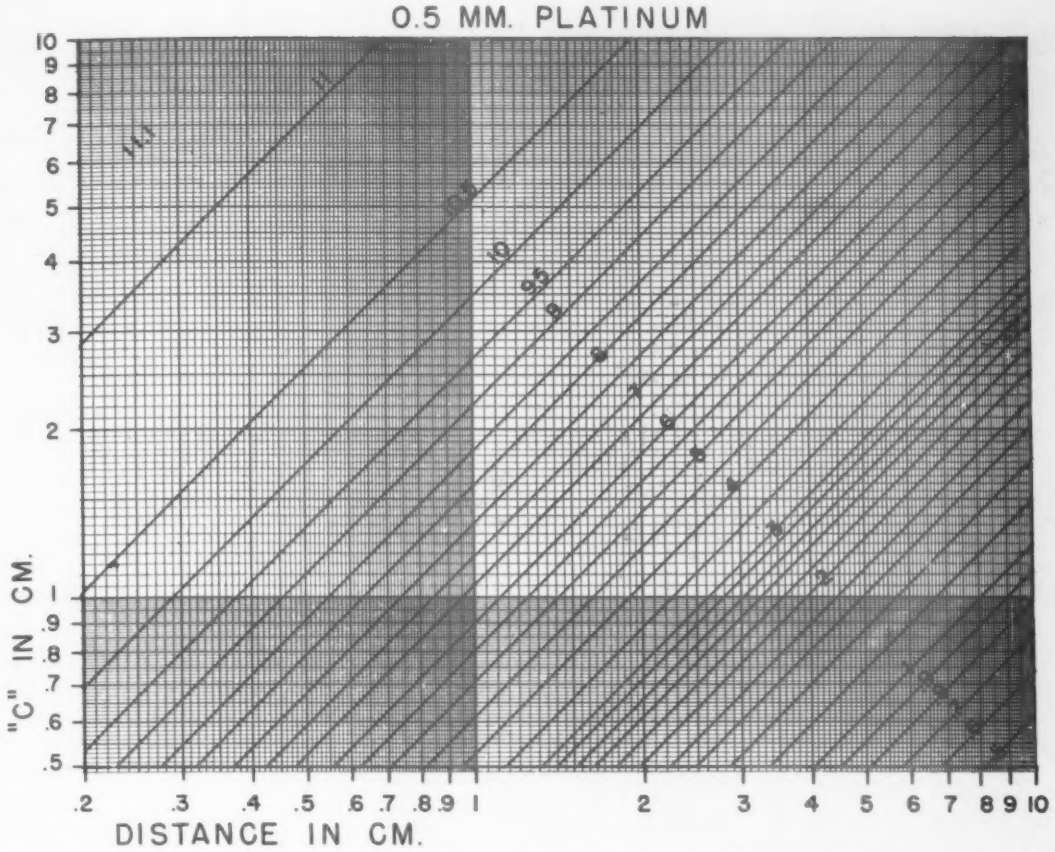

FIG. 1. Graph which gives the values of f for various values of d and c when the equivalent filtration is 0.5 mm. Pt. Find d on the horizontal coordinate axis. Find c on the vertical axis. The oblique line on which the point of intersection falls is labeled with values of f.

roentgens, the value 9.0 was used as the number of roentgens from a 1 mg. point source of unfiltered radium element at 1 cm. in one hour.

In equation form, for a linear source,

$$\text{Dose per milligram-hour} = \frac{F}{L \times d}$$

where F equals a factor, the value of which depends on the particular geometry of the problem, L = active length, d = perpendicular distance from the point at which the dose is being investigated to the central axis of the source (Fig. 3).

The problem reduces itself, therefore, to the determination of F. The value of F can be divided by L and d (or $L \times d$) and the answer obtained.

F is actually the sum of two factors, each of which is found from the graph in the same way, but separately. Or F may be said to equal $f_1 + f_2$. The value of f_1 depends on c_1 (Fig. 3) and the value of f_2 on c_2, the c values being the distances from the foot of the perpendicular to the ends of the linear source. In the graphs, values of d are plotted on the horizontal axis and values of c on the vertical axis. The oblique line, on which the point of intersection of d and c falls, gives the value of f. The values of f_1 and f_2 obtained in this way are then summated to obtain F.

In reality, F is the algebraic sum of f_1 and f_2. If the foot of the perpendicular from the point to the linear source is situated beyond the end of the source (Fig. 4), the sign of the smaller f value must be considered negative and must be subtracted from the larger f value rather than added to it in order to obtain F.

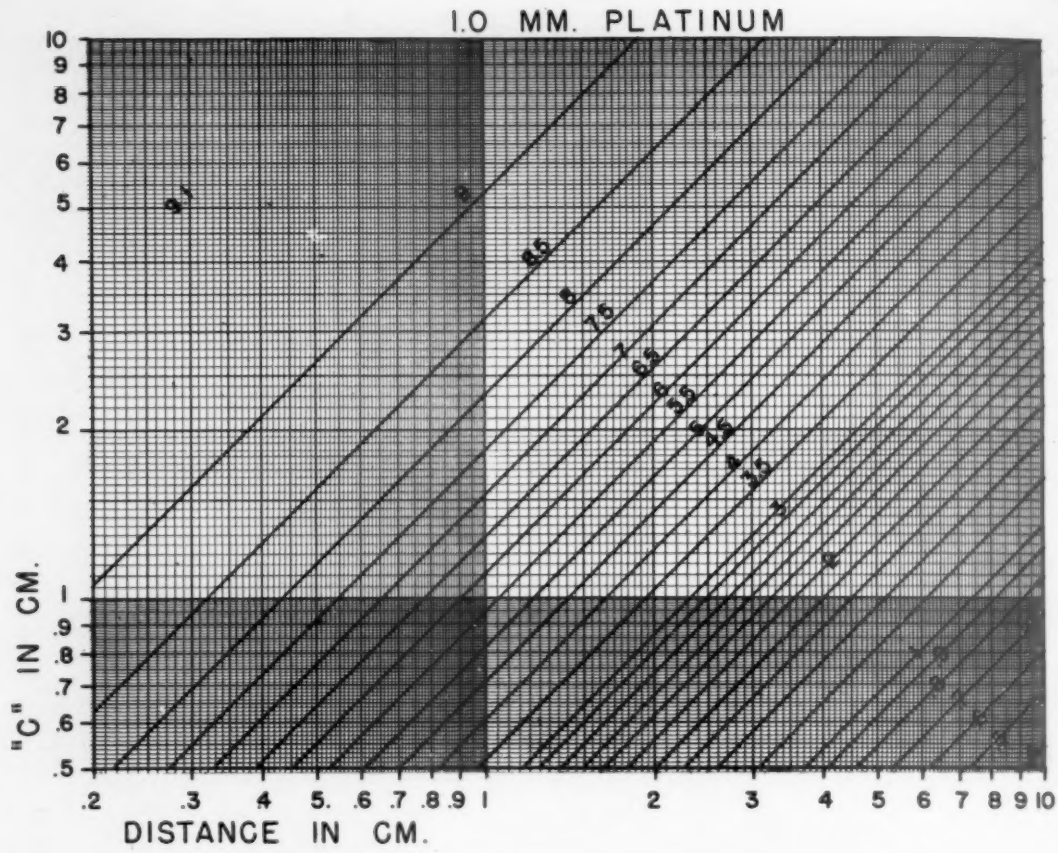

FIG. 2. Graph similar to Figure 3 but for an equivalent filtration of 1.0 mm. Pt.

Two special cases should be emphasized. If the point lies along the central perpendicular axis (Fig. 5), the c segments are each equal to one-half of L and equal to each other. Therefore, $f_1 = f_2 = f$ and $F = 2f$. If the point lies along the end or terminal perpendicular axis (Fig. 5), one of the c segments, e.g., c_2 is equal to 0 and c_1 is equal to L. Therefore, $f_2 = 0$ and $F = f_1$.

When the graphs are not available, it is useful to have an approximate formula for

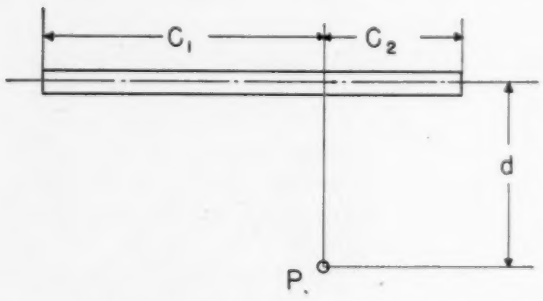

FIG. 3. d equals the distance along any axis perpendicular to the source from the point at which the dose is being investigated to the source; c_1 and c_2 are the distances between the foot of the perpendicular and the two ends of the linear source. For each of the two c values, there is a corresponding value of f. The sum of f_1 and f_2 equals F.

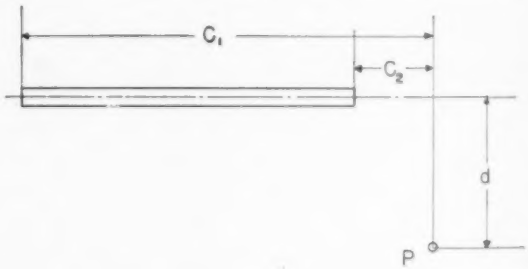

FIG. 4. The foot of the perpendicular from the point to the source falls beyond the source. c_1 and c_2 are still the distances between the foot of the perpendicular and the ends of the source, but f_2 must be subtracted from f_1 in order to obtain F.

the value of f. Such a formula for a filtration of 0.5 mm. Pt or its equivalent is

$$f = 0.138 \arctan \frac{c}{d}$$

The symbol "arctan c/d" is the angle in degrees whose tangent is equal to c divided by d. This angle may be found from the values of c and d with a single setting of any ordinary slide rule. If the angle is greater than 80 degrees, it must be assumed equal to 80 degrees in order that the error should not exceed 5 per cent. For correction factors to be used for filtration equivalents other than 0.5 mm. Pt, Table 1 should be consulted.

Table I

FILTRATION CORRECTION FACTORS

1 mm. Pt.	1.5 mm. Pt	2.0 mm. Pt	2.5 mm. Pt
Ratio $\geq \frac{1}{4}$ 90%	Ratio $\geq \frac{1}{2}$ 80%	Ratio $\geq \frac{1}{2}$ 70%	Ratio $\geq \frac{1}{2}$ 64%
Ratio $< \frac{1}{4}$ 85%	Ratio $< \frac{1}{2}$ 75%	Ratio $< \frac{1}{2}$ 65%	Ratio $< \frac{1}{2}$ 57%

To obtain the dose for filtrations other than 0.5 mm. Pt, multiply by the percentage given in the table. "Ratio" refers to the atio of the perpendicular distance between the point and the ource to the active length.
s

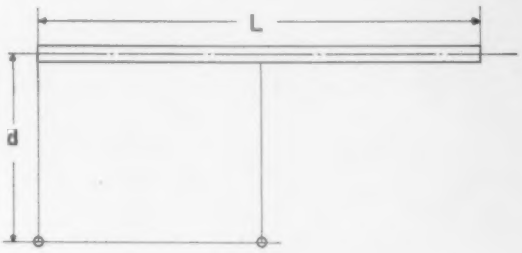

Fig. 5. L equals the active length, d is the distance along the end or central axis.

A defect in the method outlined above is the fact that the dose is not read directly from the graph. To accomplish this for all possible points, an impractical number of

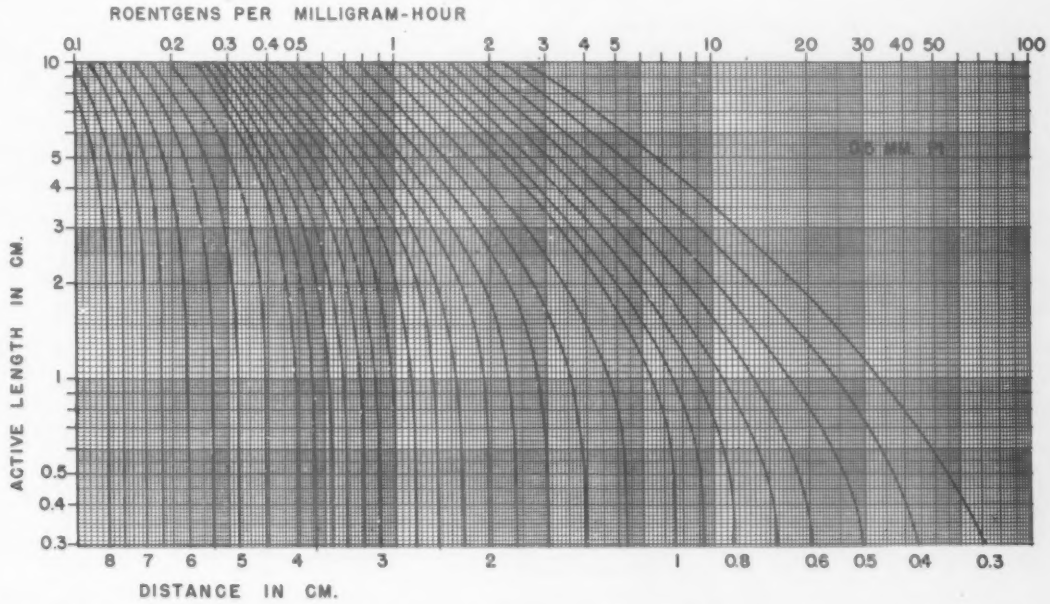

Fig. 6. Family of curves which gives the dosage in roentgens per milligram-hour along the end axis for an equivalent filtration of 0.5 mm. Pt. First, select the appropriate curve for the required distance—the curves are labeled below with their distances. The point of intersection of this curve with the horizontal line corresponding to the active length (L) is read along the scale above and gives the dose directly in roentgens per milligram-hour. To obtain the dose along the central axis, find the point of intersection of the same curve with the horizontal line corresponding to one-half of the active length ($L/2$). The dose as read on the scale above is then the dose along the central axis for the same linear source of active length L, at the same distance.

graphs would be required. In actual practice, moreover, the dosage along the central and end axes are the ones usually desired since they frequently are the minimum and maximum doses. It is possible to graphically record the doses along both these axes for any given filtration in one family of curves in such a way that the dose can be read directly. Figure 6 is such a family of curves for an equivalent filtration of 0.5 mm. Pt. Each individual curve of the group gives the dose for a particular perpendicular distance from the point to the source. The active length is plotted along the vertical axis (ordinates) and the dose in roentgens per milligram-hour is read on the horizontal axis. (The curves are drawn on double logarithmic paper in order to cover a large range of dosage.)

In reality, Figure 6 gives the values for the dose along the terminal perpendicular or end axis (Fig. 5). For example, suppose one desires to know the dose along the end axis 2 cm. away from a linear source of active length 4 cm. filtered by 0.5 mm. Pt. From Figure 6, this is 1.10 roentgens per milligram-hour. To find the dose along the central perpendicular axis (Fig. 5), one proceeds as follows:

The central axis is assumed to be the end axis for each of the equal segments into which the central axis divides the source. Since the radium is supposed to be distributed uniformly, each of the two segments contains one-half of the total radium or, if the source represents 1 milligram-hour, each segment represents 0.5 milligram-hour. The length of each segment equals 4 divided by 2, or 2 cm. From Figure 6, the dose from one segment of length 2 cm. and 2 cm. away along its end axis (in reality, the central axis of the original full source) is 1.62 roentgens per milligram-hour. Since each segment represents one-half of a milligram-hour, the dose due to each segment is one-half of 1.62 or 0.81 r. Since there are two segments, the dose per milligram-hour of the full source along its central axis is two times 0.81 or 1.62 r per milligram-hour. It can now be seen that what we have done is to read from the graph the dose per milligram-hour along the end axis of a source half the original length and both divided and multiplied it by two—i.e., we have not changed it at all. In other words, the dose per milligram-hour along the central axis of a source L cm. long is equal to the dose per milligram-hour along the end axis of a source $L/2$ cm. long at the same distance. This principle may be used for any axis (see the examples given later) but is more cumbersome than the use of Figures 1 and 2 along any but the central axis.

The values of Figure 6 were calculated from the data of Laurence.[1,2] They include a small average correction (about 5 per cent) for "effective" thickness of the platinum container and are therefore slightly smaller than values usually quoted.

For equivalent filtrations other than 0.5 mm. Pt, correction factors must be applied. These factors are given in Table 1 as percentages of the values for 0.5 mm. Pt. They were obtained by calculating the dosage for a group of representative lengths and distances at the different filtrations, using the tables of Sievert. The correction factor depends to some extent on the ratio of the distance to the active length. Two correction factors are therefore given for each filtration. These cover the full range with an error less than 4 per cent.

Linear sources may be considered as point sources when the distance from the source is greater than 3.5 times the active length, provided the foot of the perpendicular from the point to the source lies within the source and not beyond it. The small correction for "effective" thickness should, however, still be included in the calculations. To do this, a factor of 8.1 for 0.5 mm. Pt equivalent filtration may be used, or, when the ratio of the distance to the active length is greater than 3.5, the dose in roentgens per milligram-hour $= 8.1/d^2$.

Examples:

Given a linear source filtered by 0.5 mm. Pt, active length 4 cm.

To find the dose per milligram-hour

1. Along an axis 1 cm. from one end and 3

cm. from the other end, 2 cm. away from the source (Fig. 3).

2. Along an axis 2 cm. beyond the end of the source, 2 cm. away from the source (Fig. 4).

1. $c_1 = 1$ cm.
$c_2 = 3$ cm.
$L = 4$ cm.
$d = 2$ cm.
$L \times d = 8$
From Figure 1,
$f_1 = 3.8$
$f_2 = 7.8$
$F = 3.8 + 7.8 = 11.6$

$$\text{Dose} = \frac{11.6}{8} = 1.45 \text{ r per mg-hr.}$$

2. $c_1 = 6$
$c_2 = 2$
$L \times d = 8$
$f_1 = 9.7$
$f_2 = 6.3$
$F = f_1 - f_2 = 9.7 - 6.3 = 3.4$

$$\text{Dose} = \frac{3.4}{8} = 0.43 \text{ r per mg-hr.}$$

If we had used the approximate formula, $f = 0.138$ arctan c/d to obtain the f values,

1. $f_1 = .138$ arctan $\frac{1}{2} = .138 \times 26.5° = 3.7$
$f_2 = .138$ arctan $\frac{3}{2} = .138 \times 56.3° = 1.8$

2. $f_1 = .138$ arctan $\frac{2}{2} = .138 \times 45° = 6.2$
$f_2 = .138$ arctan $\frac{5}{2} = .138 \times 71.6° = 9.9$

Alternative method for Example 1:

For purposes of calculation, assume that the number of milligram-hours in each c segment is equal to its length in centimeters. Then the 4 cm. source representing 4 mg-hr. may be divided into two sources, one representing 1 mg-hr. and the other representing 3 mg-hr. The two sources have the same end axis.

For the c_1 segment, from Figure 6
Dose $= 1.89 \times 1 = 1.89$ r for 1 mg-hr.
For the c_2 segment,
Dose $= 1.34 \times 3 = 4.02$ r for 3 mg-hr.
Adding,
Dose $= 5.91$ r for 4 mg-hr.
or for 1 mg-hr.,

$$\text{Dose} = \frac{5.91}{4} = 1.48 \text{ r per milligram-hour.}$$

Alternative method for Example 2 (Fig. 4):

Again let the number of milligram-hours in each c segment equal its length in centimeters.

The two linear sources with the same end axis are now 6 cm. and 2 cm. long and represent 6 and 2 mg-hr. respectively.

From Figure 6 for c_1,
Dose $= 0.82 \times 6 = 4.92$ r for 6 mg-hr.
For c_2,
Dose $= 1.62 \times 2 = 3.24$ r for 2 mg-hr.
Subtracting,
Dose $= 1.68$ r for 4 mg-hr.
or for 1 mg-hr.,

$$\text{Dose} = \frac{1.68}{4} = 0.42 \text{ r per mg-hr.}$$

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Twenty-eighth Annual Meeting: 1943, cancelled.

EDITORIALS

SOLITARY BENIGN ENCHONDROMA OF BONE

SOLITARY benign enchondroma of bone has been considered a disease of fairly infrequent occurrence. This thought is probably stimulated by the single case reports that are published from time to time in the literature. Recently Jaffe and Lichtenstein[1] have reported a group of 28 cases from the Hospital for Joint Diseases, New York, in which they emphasize the clinical and roentgenographic findings in these cases of solitary benign enchondroma and consider the pathologic and especially the cytologic structure of the lesions, and the cytological changes which occur if the disease is undergoing transformation into a chondrosarcoma.

It is well known that a benign enchondroma may be present in the interior of a bone for a long time without causing any distention or obvious symptoms. However, lesions of this sort that appear in the short tubular bones, namely the phalanges, the metacarpals and metatarsals, often show distention of the bone cortex with thinning and some bulging over the overlying cortex. It is this bulging out of the overlying cortex for some distance which often leads to clinical misinterpretation of such an enchondroma, and too often these lesions are classed as osteochondroma.

It must be borne in mind, however, that a benign enchondroma may undergo malignant transformation into a chondrosarcoma, and Jaffe and Lichtenstein state that such an occurrence is not rare in connection with an enchondroma in a long tubular bone. However the transition is usually slow.

These benign enchondromas have a predilection for the limb bones. The lesion is found in bones of the hand and the foot, particularly in the former. The long tubular bones which are more frequently affected in the experience of all observers are the humerus and the femur.

These benign enchondromas usually begin their development in the metaphysis, though not always. A central chondroma beginning within a metaphysis may involve a large portion of the shaft of the bone and may even extend into the corresponding epiphyseal end of the affected bone. This extension into the epiphyseal end of the affected bone, however, does not occur until the epiphysis has fused with the shaft.

It is believed that these benign enchondromas of bone have their origin in misplaced cartilage rests, and these cartilage rests may be present in persons who have not had rickets and they may persist in the metaphyses for a long time before undergoing changes. Many, if not most, of the benign enchondromas remain unnoticed by the patient until some local trauma following which there is pain and swelling, and roentgenographic studies, if made at this time, usually reveal alterations in the phalanx characteristic of the lesion upon which has been superimposed a fracture.

The roentgenographic appearances of the lesions as seen in the phalanges are of a cyst-like, oval-shaped shadow. The lesion is usually situated centrally within the affected bone and, depending upon its size, there may or may not be distention of the cortex. However, if the lesion is situated eccentrically there may be a pronounced bulging, distention and thinning of the overlying cortex. Such enchondromas usually show a delicate radiopaque line where they abut on the uninvolved portion of the phalanx. The lesions may present a some-

[1] Jaffe, H. L., and Lichtenstein, L. Solitary benign enchondroma of bone. *Arch. Surg.*, April, 1943, *46*, 480–493.

what trabeculated appearance with fairly even densifications varying in size from a pinhead to the head of a match. Such densifications within the cystic area represent ossifications in the cartilage and are the telltale evidences of an enchondroma. Usually one sees evidences of a recent or unhealed fracture.

Solitary benign enchondroma is the most common solitary lesion affecting the phalanges. Often these benign enchondromas are misdiagnosed roentgenographically as a cyst, a giant cell tumor or osteochondroma. It is well to point out, as Jaffe and Lichtenstein have emphasized, that giant cell tumor of the phalanges is an exceedingly rare occurrence. Enchondromas which expand or distend the cortex may be misinterpreted as osteochondroma if attention is not directed to the appearance of the interior of the bone.

Jaffe and Lichtenstein point out that the only two solitary lesions which occur in the phalanges and which may simulate enchondroma roentgenographically are squamous epithelium-lined cyst and ossifying fibroma. Epithelium-lined phalangeal cyst seems to occur exclusively in the terminal phalanges of the fingers and indeed nearly always in the terminal half of such a phalanx, a site which is rare in benign enchondroma.

In Jaffe and Lichtenstein's experience ossifying fibroma occurring in the digits is located in the terminal phalanges but in the terminal phalanges of the toes, not of the fingers, a location extremely rare for solitary enchondroma.

In the metacarpal and metatarsal bones, enchondroma was encountered more often in the distal than in the proximal part of the shaft. The roentgen characteristics of benign enchondroma in the long bones are essentially those observed in the phalanges.

In an analysis of the pathologic material, Jaffe and Lichtenstein found that solitary benign enchondroma of bone varies as would be expected in respect to degree of cellularity, distribution of the cells, presence or absence of lacunas about the cells and amount and character of the ground substance between the cells, but the benign feature of the tumor cytologically was noted in the fact that the viable cartilage cells are rather small and their single nuclei definitely not plump.

The roentgenogram is a valuable guide in the diagnosis of solitary benign enchondroma. The presence of radiopaque dots or even blotches representing foci of calcification and ossification enables one to make the correct diagnosis. Particularly in the long tubular bones, and in the phalanges, the metacarpal and metatarsal bones if there is a fairly large area of rarefaction associated with thinning and bulging of the cortex one may be fairly certain that the changes are due to an enchondroma. This is true even in the presence of spotty calcification, and the relative commonness of this benign type of lesion in the phalanges, metacarpals and metatarsals would make the diagnosis of enchondroma the most likely one. It must be borne in mind that enchondroma especially of the long tubular bones may undergo malignant transformation.

CHARLES BYRON WARD, M.D.*
1882–1943

THREE score years covered the birth, development, life work and death of Dr. Charles Byron Ward. He was born of English stock on a farm near Strathroy, Ontario, in 1882. Early he had to pitch in and help himself through college and medical school. This usually develops self-reliance, initiative and a strong positive character.

After premedic work in London, Ontario,

* Reprinted from the *Bulletin of King County Medical Society*, April 19, 1943.

he attended medical school at Toronto University, graduating in 1908. Postgraduate courses at London, England, and Edinburgh, Scotland, followed. At the latter place he became acquainted with Dr. Fursey of Spokane, Wash., who induced him to move to the Pacific Northwest. Three years he practiced medicine and surgery in Spokane. About this time roentgen ray machines were beginning to find their place in diagnostic medicine and surgery. Dr. Ward had one of the early types, a huge showcase affair with revolving mica and glass discs, Leyden jar, and widely separated anodal and cathodal poles, between which jumped a lightninglike spark with a crackling like a cowboy's snake whip. From here on he kept pace with the rapid development of roentgen machines, especially those devoted to therapy. This became his field.

In 1932 his work in Spokane became so well known that he was urged to come to Seattle to organize and conduct the Tumor Institute of the Swedish Hospital. This he did with considerable success and succeeded in interesting physicists from the University of Washington.

Four years ago he resigned from this staff to open offices for private practice. At this same time he organized and headed the roentgen therapy department at Providence Hospital. Under his management this department soon became a great aid to the staff, as with increasing longevity malignant tumors are on the increase.

Dr. Ward was a member of many societies, the American College of Radiology, the American Roentgen Ray Society, the Radiological Society of North America and diplomate of the American Board of Radiology.

And what of his hobbies? He was a born organizer. While practicing in Spokane, he saw the need for a modern medical library easily available to the doctors. It was through his planning and efforts that a substantial sum of money was raised to equip and sustain an excellent library with clubrooms adjacent. When he moved to Seattle, the King County Medical Society Library was located in cramped quarters in the Stimson Building and there was no trained librarian.

Immediately he became interested in the reorganization of our library. The result was larger and beautifully appointed quarters in the Cobb Building. He made extensive visits to many medical libraries throughout the country to obtain ideas and plans suitable for our own society. He was insistent that a trained librarian be appointed and was largely instrumental in securing the services of Miss Ruth Harlamert, who has so ably built up our library in usefulness and popularity. Those who have closely watched this library from its early beginnings, through its struggles to survive and down to its present condition of steel stacks, multiple indices, reference service, steady income, completion of unbound journals, study cubicles and modern magazine racks, realize that a strong hand has been guiding it.

Charles Ward has left us much. We are indebted to his breadth of vision, his foresight and his generosity. His death on March 27 was a shock to all of us. We will miss him sorely, but often think of the fine contributions he has made for the advancement of medicine. A. J. P.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual Meeting: 1943, cancelled.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: 1943, cancelled.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Drake Hotel, Chicago, Ill., Nov. 29–Dec. 3, 1943.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. J. D. Coate, 434 Thirtieth St., Oakland, Calif.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL ASSOCIATION
Secretary, Dr. Donald R. Laing, 65 North Madison Ave., Pasadena, Calif. Meets on second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. Warren W. Furey, 6844 S. Oglesby Ave., Chicago, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. J. O. Newton, 13921 Terrace Rd., East Cleveland. Meets at 6:30 P.M. at Midday Club on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. Edward J. Meister, 366 Metropolitan Bldg., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Building.

FLORIDA RADIOLOGICAL SOCIETY
Acting Secretary, Dr. Walter A. Weed, 204 Exchange Bldg., Orlando, Fla. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month at a place designated by the president.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Hugh F. Hare, Lahey Clinic, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. H. H. Kasabach, Presbyterian Hospital, New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. R. P. Barden, University Hospital, Meetings first Thursday of each month from October to May inclusive at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. R. G. Alley, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Sidney Larson, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
Secretary, Dr. P. C. Schnoebelen, 462 N. Taylor Ave. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. Herman Klapproth, Sherman, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October throughMay, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. D. Irvine, 540 Tegler Bldg., Edmonton, Alberta.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse Biel. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

CANCER TEACHING DAY

A program under the title of Cancer Teaching Day and arranged under the auspices of a number of medical societies of the State of New York will be presented at the Homer Folks Tuberculosis Hospital, Oneonta, New York, on Thursday, October 7, 1943. The meeting will be called to order at 4:00 P.M., and the following program will be presented:

Opening Remarks. Mahlon C. Halleck, M.D., President, Medical Society of the County of Otsego.

Care of the Incurable Cancer Case. Norman Treves, M.D., New York, N. Y.

Cancer of the Cervix. Gray H. Twombly, M.D., New York, N. Y.

Cancer of the Larynx, Bronchi, and Esophagus. Chevalier L. Jackson, M.D., Philadelphia, Pa.

Dinner will be served at 6:15 P.M. at the Homer Folks Tuberculosis Hospital. Reservations are required in advance and it is requested that those planning to attend the dinner send their reservations to Dr. Ralph Horton, Superintendent, Homer Folks Tuberculosis Hospital, Oneonta, New York.

The program will be resumed in the evening at 7:30 P.M., and the following papers will be presented:

Cancer of Face and Lip. Andrew H. Dowdy, M.D., Rochester, N. Y.

Roentgen-Ray Aspects of Bronchogenic Carcinoma. George N. Scatchard, M.D., Buffalo, N. Y.

RADIOLOGICAL SOCIETY OF NEW JERSEY

At the annual meeting of the Radiological Society of New Jersey held at the Essex House, Newark, New Jersey, on May 26, 1943, the following officers were elected for 1943–1944: *President*, Dr. H. A. Vogel; *Vice President*, Dr. J. H. Wyatt; *Secretary*, Dr. H. J. Perlberg; *Treasurer*, Dr. W. H. Seward; *Councillor*, Dr. W. O. Wuester.

AMERICAN BOARD OF RADIOLOGY

There will be no fall examination of the American Board of Radiology. The next examination will probably be conducted in February, 1944. Those wishing to appear for examination at that time must file their application by December 15, 1943.

B. R. KIRKLIN, *Secretary*
American Board of Radiology
Mayo Clinic, Rochester, Minn.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

A Bibliography of Aviation Medicine. By Ebbe Curtis Hoff and John Farquhar Fulton. Prepared for the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, Acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Cloth. Price, $4.00. Pp. 237. Springfield, Illinois: Charles C Thomas, 1942.

The reviewer who, for several reasons, has a deep interest in aviation and all matters pertaining to it, sat down to a perusal of "A Bibliography of Aviation Medicine" with every prospect of being mildly bored by the performance of an assignment to which he had been committed. His acquaintance, however, with one of the authors, Dr. Fulton, which began when the latter was a medical student, guaranteed at least two things: one, that the job would be done with a high degree of accuracy and thoroughness, and the other, that interspersed with what would sometimes seem to be the dull recital of 5,736 pertinent references would be brilliant comments and a gratifying arrangement of material which could only be accomplished by one who not only has a profound and comprehensive knowledge of medicine and the medical sciences but also has the knack of expressing himself attractively, tersely, and clearly.

Such a compilation is indeed timely, for, as is stated in the preface, the technological developments of aircraft have reached the stage where the stresses imposed on flight personnel tend to limit further development of aviation. The strain placed upon the aviator who is flying in combat at such heights as 40,000 feet has so seriously taxed the human body that it has given rise to the new branch of aviation medicine. The growing literature on this subject which deals with medicine, as well as the biological, physical and chemical sciences, has already become so extensive that a compilation of the literature becomes imperative if full advantage is to be taken of the knowledge which has already been accumulated in this field.

The authors have consulted some eight hundred journal files and have truly made the investigation world-wide for references have been incorporated from the English, German, Russian, Polish, Spanish, Portuguese, Italian, French, Hungarian, Yugoslavian, and Japanese. An attempt has been made to include all of the more important and accessible articles up to January 1, 1942, when the material was prepared for press. Some additional titles, however, were added after this date but none later than May 31, 1942. With the almost daily advances in this field, it is hoped that a supplement to this initial contribution will be added annually.

The references are grouped into fourteen different divisions as follows: history and general aspects of aviation; the special physiology of aviation and conditions simulating flight; the special pharmacology of aviation and conditions simulating flight; the special psychology of aviation and conditions simulating flight; aeromicrobiology (bacteriology and immunology in aviation and high altitudes); diseases and accidents in aviation and conditions simulating flight; selection and assessment of efficiency of flight personnel; training performance and fatigue of flight personnel; protection of flight personnel; preventive medicine and therapeutics of aviation; aviation and public health (sanitary aviation); organization of aviation medicine; special problems (including such subdivisions as rapid decompression, shock and vibration, parachute jumping, aviation medicine and the law, life insurance for flyers, etc., etc.); general studies in aviation medicine; and bibliographies. In addition, a complete index of authors and of subjects is given. Each one of the main sections has many important subdivisions which cover the subject in a most comprehensive manner but no attempt can be made here to indicate in detail the extent of the material covered except to say that it appears to be most thorough in its scope.

Such a bibliography is a much needed and invaluable aid to the physician for whom some knowledge of aviation medicine is desirable, to

the teacher in medical schools who now must inaugurate courses dealing with this new and important aspect of medicine, and for the research worker who must familiarize himself with the work of preceding investigators if he is to proceed intelligently with his own problems in this field.

CYRUS C. STURGIS

WAR GASES: THEIR IDENTIFICATION AND DECONTAMINATION. By Morris B. Jacobs, Ph.D., Food, Drug and Insecticide Admin., U. S. Dept. of Agr., 1927; Chemist, Department of Health, City of New York, 1928; Formerly, Lt. U. S. Chemical Warfare Service Reserve. Cloth. Price, $3.00. Pp. 180, with 8 illustrations and numerous tables. New York: Interscience Publishers, Inc., 1942.

The object of this manual is to offer information, mainly on the analytical chemistry of war gases, to those interested in civilian defense. It is based on the available publications up to 1941, official and unofficial, which are frequently cited. The author does not, however, presume to give the official views of any branch of the Government.

Dr. Jacobs, favorably known for his book, "The Analytical Chemistry of Industrial Poisons, Hazards and Solvents," has done a worthy job of systematizing the present subject for ready reference under seven major sections, viz.: classification of chemical agents; the physical characteristics and physiological response of the war gases; effect of war gases on materials, water and food; scheme of analysis; detection and determination of arsenic; confirmatory tests; decontamination.

The subject matter is presented clearly and simply, and contains much information of value to the general reader as well as to the health officer and the decontamination officer. The latter will, of course, have the benefit of official instructions, usually revised to include the latest practical and experimental information; nevertheless, this should not detract from the timeliness and inherent general value of this manual.

BARNETT COHEN

OLEOPERITONEOGRAFIA: CONTRIBUCIÓN AL ESTUDIO RADIOLÓGICO DEL PERITONEO. POR LOS DOCTORES Prof. Carlos H. Niseggi, Profesor Adjunto de Radiología de la Facultad de Medicina de Bs. Aires; Jefe del Servicio Central de Radiología del Hospital Teodora Alvarez; Miembro Fundador de la Sociedad Argentina de Radiología; Marcelo H. Moreau, Médico Agregado del Servicio Central de Radiología del Hospital Teodoro Alvarez; Miembro Titular de la Sociedad Argentina de Radiología, and Jorge E. Moreau, Médico Interno del Instituto Municipal de Radiología y Fisioterapia. Paper. Pp. 197, with 153 illustrations. Buenos Aires: "El Ateneo," 1941.

The authors discuss and illustrate the development of their roentgenologic method of studying peritoneal effusions after the injection of 3 cc. of 40 to 50 per cent iodized oil. The technique has been found to be of value in differentiating ovarian cysts, for example, from other lesions producing peritoneal effusions, and in diagnosing other types of cysts and hydrosalpinx. The roentgenograms of forty illustrative cases are presented, but they suffer from imperfect reproduction. This monograph is of interest in that it offers a roentgenologic substitute for the peritoneoscope.

E. T. LEDDY

DIE DIFFERENTIALDIAGNOSE DER WIRBELSÄULENTUBERKULOSE. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, Ergänzungsband 60.) Von Priv.-Doz. Dr. J. E. W. Brocher, Genf. Paper, price, RM. 14.70; bound, RM. 16.20. Pp. 88, with 129 illustrations. Leipzig: Georg Thieme, 1941.

This monograph is written especially for the beginner in roentgenology and therefore stresses the differential diagnostic viewpoint to the extent of including some conditions which the experienced roentgenologist would not mistake for tuberculosis. A brief review of the clinical methods of examination of the patient suffering from some disturbance of the spine is followed by a short discussion of tuberculous spondylitis, of nontuberculous spondylitis, of Scheuermann's disease, of symptoms due to "wear and tear," of anomalies of the spine, of osteoporosis and osteitis fibrosa. The author also covers briefly vertebra plana, post-traumatic gibbus formation and tumors. He then relates briefly the importance of the roentgenogram for the clinical diagnosis. Although he fully realizes that diagnostic criteria cannot be condensed into an ideal schematic form he offers a tabulation of the anomalies outlined in the book under the subheadings of (1) roentgen findings, (2)

underlying pathology, (3) pathological signs or symptoms. A brief chapter on therapy and a short bibliography conclude the text. The 129 illustrations are well chosen and very instructive.

Ernst A. Pohle

Laboratory and Clinical Studies. Vol. XXI. From the Memorial Hospital, Huntington Fund for Cancer Research; Douglas Research Laboratory, New York City: 1940.

The 1940 volume of the consolidated writings of the Memorial Hospital staff members is made up of fifty reprints of articles dealing with a wide variety of problems all related in some way to the central theme of cancer research. This paper-bound publication, in keeping with its predecessors from the same source, is a rich storehouse of detailed information.

From a perusal of the historical facts surrounding the treatment of laryngeal cancer in the case of Frederick III of Germany, by Pack and Campbell, to the Janeway Lecture of 1939, by Failla, dealing with some aspects of the biological action of ionizing radiations, almost every phase of thinking regarding the entire cancer problem is represented in this group of fifty reprints. The Memorial Hospital Laboratory and Clinical Studies series is best judged as a continuing flow of scientific contributions rather than upon the basis of any one particular volume.

Fred J. Hodges

Selected Papers from the Royal Cancer Hospital (Free) and the Chester Beatty Research Institute. Vol. I, 1935–1939. Paper. Price, 16/-. Pp. 484, with numerous illustrations. London: Royal Cancer Hospital (Free).

This is not like a book written by a single author and cannot be reviewed as such. The volume contains a series of papers which originally had appeared in different technical periodicals between 1935 and 1939 and which have been gathered into a single volume for the convenience of many readers. Although not formally divided into specific parts, the material is arranged into four groups: the papers of the first group deal with clinical subjects including the surgical treatment of cancer of the rectum by Miles; Hashimoto's disease by Joll; a classification of cancer of the breast by Raven; multiple tumors of the brain secondary to bronchial carcinoma by Carnegie Dickson and Worster-Drought; and multiple meningeal and perineural tumors by Worster-Drought, Carnegie Dickson and McMenemey. The papers of the second group are all by Mayneord alone or in collaboration with Roberts, Clarkson, or Honeyburne, and deal with radiological physics, notably with the significance of the roentgen. To those who are interested in the physics of radiology these papers are important because each subject is set forth and discussed with critical clarity which characterizes all of Mayneord's writings. In the two papers of the third group Woodburn-Morison and Mayneord discuss low voltage roentgen therapy, and Flood and Smithers describe in detail their method of low voltage roentgen therapy at short distance. The fourth group includes seventeen articles, most of which deal with the production of tumors by various carcinogenic agents or with biological phenomena. The publication of this collection will be appreciated by all those who are seriously interested in cancer and its treatment.

A. U. Desjardins

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

GYNECOLOGY AND OBSTETRICS

GRABER, EDWARD A. A simple method of x-ray pelvimetry. *Am. J. Obst. & Gynec.*, May, 1941, *41*, 823–830.

A method of pelvimetry is described which can be used by every physician who handles obstetric cases. The many excellent methods of pelvimetry already available are so complicated that the average practitioner cannot master or readily adopt them.

Three roentgenograms of the pelvis are taken: (1) a horizontal anteroposterior; (2) a horizontal lateral, and (3) a 45° angle exposure of the subpubic arch and side walls. A ruler is placed between the buttocks when taking the lateral exposure. Since the ruler lies in the midline, its image on the film will be distorted in the same proportion as all the anteroposterior measurements taken in this plane. Thus, on the lateral film one needs only to measure the distance between the anterior and posterior landmarks of the inlet, midplane or outlet and transpose the distance on the image of the ruler on the plate and then read the true measurement.

To obtain the transverse diameters of the pelvic planes, the distances between the various landmarks should be measured directly on the anteroposterior roentgenogram. However, since the transverse planes of the inlet, midplane, and outlet lie at different distances from the roentgen tube, the degree of distortion of each is different. This can be corrected for if the distance from the plate to the transverse plane to be measured is known. The lateral roentgenogram is now consulted and a baseline is drawn parallel to the film edge that touches the most lateral border of the sacrum. This represents the table top if the patient was lying on her back. In order to find how far the plane is from the table top, one need only measure the distance from the plane to the base line and read the result directly from the ruler image on the plate. A table is then consulted (Table 2 in the article) and by using both the table-top-plane measurement and the transverse measurement of the image on the anteroposterior roentgenogram, the true transverse measurement can be determined.

Another table (3) is given so that the inexperienced physician may have some system of evaluating the pelvis and some basis for his judgment of its capacity. It includes the average normal pelvic measurements.

The measurement of the head has not been particularly successful chiefly because the fronto-occipital is the only diameter that can be measured and this is not the diameter that engages.

With good pelvic construction, every woman with an average sized baby who has an obstetric conjugate of 9 cm. is entitled to the chance of delivery from below. An obstetric conjugate of 8 cm. is considered an absolute contraction.—*Mary Frances Vastine.*

THOMS, HERBERT. The Naegele pelvis. *Am. J. Obst. & Gynec.*, May, 1941, *41*, 830–836.

Three Naegele pelves have been found within two years in a relatively small clinic. This suggests that this deformity is much more widespread than is popularly supposed. Williams observed in 1926 that probably less than 100 instances have been described in the literature.

Over one hundred years ago, Franz Carl Naegele described the deformity as a "pelvis contracted in one of the oblique diameters with complete ankylosis of the sacroiliac synchondrosis on one side, combined with imperfect development of the sacrum and os innominatum on the same side." In many instances, knowledge of the condition is unknown until, for one reason or another, a roentgenogram of the pelvis is made. The obscurity of the diagnosis is probably due to the absence of obvious external deformity or change in gait. However, variations in the height of the iliac crests and an accompanying scoliosis are suggestive findings. The transverse diameter of the outlet is always diminished, usually markedly, so that there is a definite sense of constriction in examining vaginally. Laterally the pelvic side wall on the affected side is readily felt on vaginal examination and is found to be displaced toward the body midline.

Two of the cases described gave a history of full-term pregnancies successfully delivered. The author concludes that the importance of the routine procedure which he has carried out for the past six years, namely that of performing roentgen pelvimetry on every primigravid woman, has again become obvious.—*Mary Frances Vastine.*

TORPIN, RICHARD. Naegele pelvis: study of a case in labor. *Radiology*, March, 1942, *38*, 330–332.

There has been a great deal of discussion as to whether Naegele pelvis—the obliquely ovate pelvis—is a congenital condition or is caused by inflammation. Breus and Kolisko in their work on deformed pelves stated that it is always inflammatory in origin.

A case is described in a negro primipara eighteen years of age sent to the hospital in the second stage of protracted and difficult labor. The roentgenograms of the case are presented. They showed the left ala of the sacral bone apparently entirely absent, resulting in inward displacement and deformity of the left innominate bone. There was no evidence of injury or inflammation and the perfect regularity of the bone fibers indicated that the condition was congenital rather than inflammatory. This was supported by the history which showed no injury or disease of the pelvis. The patient began to walk at nine months of age and said that she never tired of walking and dancing. There were no scars or external deformities and pelvic trouble had never been suspected.—*Audrey G. Morgan.*

SKELETAL SYSTEM

COOPER, ERIC L. Familial acholuric jaundice associated with bone changes. *Ann. Int. Med.*, Nov., 1941, *15*, 858–868.

A new family with familial acholuric jaundice is reported from Melbourne, Australia. Three families with this disease have been reported previously from this city of practically one million inhabitants. Ten individuals in three generations of this latest family have been affected with the disease. Three of the cases are described.

They show intermittent attacks of jaundice and fragility of the red blood cells. The spleen is enlarged. Splenomegaly is performed, often with good results, in the treatment of the disease. The patients here described presented mongoloid facies, enlarged heads with very thick skull bones and thick, muddy yellow skin. The roentgenogram of the skull showed fine lines of denser bone radiating at right angles to the inner table. There was also an appearance similar to that seen in brain tumors and described as hammered copper markings. Hyperplastic red bone marrow had largely replaced the osteoblastic tissue and most of the thickness of the skull bones consisted of masses of marrow separated by fine strands of bone.

Many other anemias are associated with active erythropoiesis but very few begin so early in life. The three blood dyscrasias, acholuric jaundice, sickle cell anemia and erythroblastic anemia may begin in early infancy or even during intrauterine life.—*Audrey G. Morgan.*

WASSERSUG, JOSEPH D. Tuberculosis of ribs. *Am. Rev. Tuberc.*, Dec., 1941, *44*, 716–721.

Among 1,134 cases of bone and joint tuberculosis studied at the Lakeville State Sanatorium, the incidence of tuberculosis of ribs was 1.14 per cent. Males were so involved three to five times more commonly than females. Usually only one rib was concerned and there appeared to be no definite selectivity either as to side or rib.

Clinically, the onset of the infection was very insidious or characterized by swelling and pain. One or more sinus tracts developed. With such evidence, the author recommends tuberculin tests, serological examinations and roentgen studies including sinus tract injections.

Rib resection appears to be the most practical type of treatment.—*A. A. de Lorimier.*

STRAUSS, HYMAN, and MCGOLDRICK, JOSEPH L. Fracture of the femoral neck following roentgen therapy for gynecologic malignancy. *Am. J. Obst. & Gynec.*, June, 1941, *41*, 915–933.

A discussion of fracture of the femoral neck as a complication of irradiation for pelvic malignancies appeared for the first time in the American literature in 1936 in an article by Dalby, Jacox and Miller. The authors review all the reported cases and present 4 of their own.

The cases of cervical carcinoma presented each received from 2,400 to 3,000 roentgens to each of six pelvic fields (including two lateral) making a total of from 14,400 to 18,000 r (measured in air). In addition, each patient received radium to the cervix, the dosage of

which varied from 4,000 to 6,500 mg-hr. The intracapsular fractures which followed were diagnosed respectively in the 4 patients at six, eleven, twenty and twenty-four months following the completion of therapy. Two of the patients were sixty-four years of age, one was fifty-eight and one was thirty-five. In each instance, the onset of symptoms was insidious. The right femur was involved in 2 cases, the left in one and the fracture was bilateral in one patient. Subsequently, one patient (the youngest) died and careful histopathologic examination of multiple sections from the fracture site and adjacent bone revealed no metastatic involvement.

The authors conclude that the small increase of depth dose resulting from treatment through lateral fields does not justify the added risk incurred. The vascular supply of the femoral neck is terminal and vulnerable to post-irradiation vascular occlusion. In addition, many of the patients with pelvic cancer are poorly nourished due to a calcium-phosphorus-vitamin imbalance.—*Mary Frances Vastine.*

Krause, George R. March fracture. *Radiology*, April, 1942, *38*, 473–476.

March fracture or march foot is caused by prolonged foot strain in walking or marching long distances. There may be other predisposing causes such as myositis, periostitis, disturbed circulation or bacterial infection. With the present military situation doubtless many more of these cases will be seen. The author has seen 9 cases in the past six months at Station Hospital, Fort Jackson, S. C.

The onset is generally gradual, though some patients have reported sudden pain. There is slight discomfort in the metatarsal region when weight is borne on the foot, which may increase to severe pain which is relieved by rest and elevation of the foot. The patient limps and there is edema of the back of the foot. Diagnosis is usually made by roentgen examination but the roentgenograms must be technically perfect to make an early diagnosis. In the first stage, which lasts about ten days, there may be a narrow incomplete fracture line which is apt to be overlooked unless the roentgenogram shows maximum detail. In the second stage, one to three weeks after the beginning of symptoms there is a faint, slightly calcified, fuzzy callus around the distal end of the second or third metatarsal. In the third stage, after immobilization, the callus is denser, more sharply circumscribed, and looks harder. The fracture line is often still visible. This stage covers another period of three to six weeks. In the fourth stage, after several months, the only visible sign is a slight thickening of the cortex.

One of the author's cases is described in detail and illustrated with roentgenograms showing the four stages.—*Audrey G. Morgan.*

Rost, Glenn S. Roentgen manifestations of bejel ("endemic syphilis") as observed in the Euphrates River Valley. *Radiology*, March, 1942, *38*, 320–325.

Bejel is a treponematosis that is endemic in the Euphrates River Valley. It has many resemblances to syphilis and yaws and occurs most frequently in childhood. This roentgen study of the disease was made at the Medical Center of Deir-ez-Zor, Syria.

The early bone lesions are thickening of the periosteum and increased size of the bone. The long bones, particularly the tibia and ulna, are most frequently affected but any bone may be involved. Later a "lace work" pattern like that of acquired syphilis may develop. There may be lesions resembling gummata, generally associated with increased density and thickening of the cortex. The proportion between bone destruction and new formation of bone varies in different cases and different stages of the disease.

The early bone lesions of heredosyphilis have not been seen in bejel. There are no lesions of the heart and great vessels such as those seen in syphilis nor are the neuropathic joint lesions, known as Charcot joint, seen. Blood serology was positive in most of the cases and they responded to antisyphilitic treatment. The exact relationship between this disease and yaws and syphilis cannot yet be defined.—*Audrey G. Morgan.*

Jones, Horace C., and Hedrick, Donald W. Patellar anomalies, roentgenologic and clinical consideration. *Radiology*, Jan., 1942, *38*, 30–34.

Seven cases of anomaly of the patella are described and roentgenograms given of the various forms of anomaly, such as bipartite or multipartite patella, transverse and vertical fissures and linear fragmentation at lower pole. There is still disagreement as to the cause of these anomalies, some attributing them to failure of ossification centers to coalesce and

others to osteochondritis. Possibly both factors are involved.

Differential diagnosis between congenital anomaly and fracture of the patella is sometimes important from the medicolegal point of view. Differentiation can generally be made from the history and the clinical and roentgen findings. In anomaly the adjacent surfaces are uniformly separated throughout their length and the edges are smooth, while in fracture the space between the fragments is of varying width and the edges are jagged. A fracture is rarely seen in the upper, outer quadrant, and is almost always unilateral, while in anomaly the fissure is almost always in the upper and outer quadrant and is often bilateral. Bilateral roentgenograms are of value in establishing the differential diagnosis. Rest and immobilization generally are sufficient treatment. Surgery for removal of a fragment is rarely necessary. The condition should be diagnosed in early adolescence and measures taken to avoid undue strain on the extensor muscles.—*Audrey G. Morgan.*

OPPENHEIMER, ALBERT. Calcification and ossification of vertebral ligaments (spondylitis ossificans ligamentosa): roentgen study of pathogenesis and clinical significance. *Radiology*, Feb., 1942, *38*, 160–173.

The author made a clinical and roentgen study of 282 persons between the ages of fourteen and eighty-four years who had definite calcification or ossification of vertebral ligaments. The mobility of the vertebrae was tested in every case and recorded on photographs or roentgenograms. The study was made for the purpose of answering some of the disputed questions in regard to this condition, such as the conditions under which the ligaments calcify or ossify, the relationship of the calcification or ossification to lesions of the bodies of the vertebrae, the intervertebral discs and the apophyseal joints, and whether the calcifications or ossifications cause stiffness of the back, pain and root symptoms. Roentgenograms of illustrative cases are given.

He concludes that lime salts may be deposited in the vertebral ligaments when their tension or mobility is decreased. Calcification or ossification of the ligaments does not cause decreased mobility of the vertebrae but sometimes result from it. Even though the ligaments are calcified or ossified the mobility of the vertebrae remains normal unless the apophyseal joints or the bodies of the vertebrae themselves are diseased. There may be complete rigidity of the spine in Strümpell-Marie's disease without any calcification or ossification of the ligaments. Often the ligaments do not ossify or calcify until after the spine or certain segments of it have been rigid for some time.

Calcification and ossification of the longitudinal ligaments does not cause pain. If the ligamenta flava are calcified or ossified they may cause pressure on the nerve roots and therefore root pain. But they may be calcified or ossified without causing any clinical symptoms at all.

Calcification or ossification of vertebral ligaments follows many kinds of lesions of the spinal column but is not characteristic of any one. Therefore it is not an independent disease but is secondary to a number of other diseases. If present it indicates a lesion of the vertebrae or apophyseal joints and a careful search should be made for the underlying cause.—*Audrey G. Morgan.*

GENERAL

CHAMBERLAIN, W. EDWARD. Fluoroscopes and fluoroscopy: Carman Lecture. *Radiology*, April, 1942, *38*, 383–413.

In this Carman Lecture the author says that fluoroscopy is very much the same as it was when Carman's book appeared in 1917 and the 1941 models of commercial fluoroscopes are not very different from those sold at that time. But he describes two models, a biplane and a multiplane fluoroscope, constructed under his direction at Temple University and points out their advantages.

However, the inadequacy of clinical fluoroscopy lies not so much in defects in the apparatus as in functional limitations of the human retina. The question of the physiology of the retina is discussed in detail and curves illustrating the subject given. A study of this question of retinal physiology leads to the conclusion that for adequately clear fluoroscopic images it will be necessary to increase brightness about 1,000 fold. This he believes will be accomplished and within a relatively short time.

In the meantime the fluoroscopist should make a careful study of his technique and of the question of dark adaptation. Adaptometers

for accomplishing this purpose are illustrated. It is necessary to consider not only visual acuity but also intensity discrimination. He can also determine the degree of brightness with which he is working with tissues of varying thickness, and from that how poor his intensity discrimination and visual acuity are under given circumstances. In cases in which visual acuity is more important than intensity discrimination he can increase the former by wearing lenses of 3 to 6 diopters.

Some of the fluoroscopes in use today are inferior and should be changed. Target-screen distances should never be less than 18 cm. and 26 cm. is better. A tube for clinical fluoroscopy should be capable of operating at 120 kv. (peak) on a full-wave, 4-valve-rectified transformer. It should be of the shock-proof, cable-connected, oil-insulated type. It should be provided with some positive method of cooling the housing. The anode-stem should be hollow and should have some method of forcing cool oil against the copper as near as possible to the focal spot. It should have a booster capable of changing it from a low to a high energy setting.

Whether or not complete rod vision could be attained, the time required for dark adaptation could be greatly shortened by excluding daylight from the dark room. Various colors of artificial illumination which are favorable to dark adaptation are being tested. A few minutes of dark adaptation will accomplish as much as is ordinarily accomplished in thirty or forty minutes if the observer has been protected from the more actinic wave lengths for a number of hours before he enters the fluoroscopic room.—*Audrey G. Morgan.*

Brown, Percy. The inception and development of fluoroscopy: the influence of Carman on its status in America. *Radiology*, April, 1942, *38*, 414–425.

This is the Russell Carman Memorial Lecture for 1935 published in *Minnesota Medicine* and reprinted here at the request of Dr. Chamberlain who delivered the Carman Lecture for 1941. He wished the Brown lecture to be reprinted as a history of the life and work of Carman while his own article served as what he called a technical appendix to it.

This lecture reviews the whole history of fluoroscopy up to that date and particularly the immense stimulus and encouragement to it furnished by Dr. Carman's work at the Mayo Clinic. One of his outstanding contributions was his demonstration of the value of fluoroscopy associated with palpatory pressure and he must have been particularly gratified by two developments which showed its value. The first was that of the development of Forssell's work on relief demonstration of the folds of mucosa in the digestive tract which necessitated fluoroscopy under palpatory pressure and the second was the discovery of the meniscus sign of ulcerating gastric cancer which could not have been accomplished without this method. —*Audrey G. Morgan.*

Braestrup, C. B. X-ray protection in diagnostic radiology. *Radiology*, Feb., 1942, *38*, 207–216.

Efficient protection has been provided in high voltage therapy installations. The chief danger to personnel lies in the use of roentgen apparatus for diagnostic purposes, particularly as it is often used by physicians who have not specialized in roentgenology and do not realize the danger.

The protective materials used in so-called ray-proof apparatus are discussed and tables given showing the amount of stray radiation from various types of diagnostic tube enclosures. Mobile units have proved particularly harmful as they are often used for fluoroscopy by surgeons who do not realize the high output at short distances.

It is evident that there should be a periodic check on the amount of stray radiation received by the personnel of the roentgen room. A table is given showing the figures for one hospital in which no one received a dose of more than 0.2 r per month, leaving a large margin of safety. An accurate check may be made by means of a pocket ionization chamber or an approximate but satisfactory one by carrying dental film in the pocket for a month. These film determinations are dependable enough to show whether more accurate ionization measurements are necessary.

In diagnostic roentgenology there is more danger from ignorance or carelessness on the part of the personnel than there is from the equipment or defective shielding. If the roentgenologist and his staff are not trained to take precautionary measures satisfactory protection is impossible.—*Audrey G. Morgan.*

ROENTGEN AND RADIUM THERAPY

DESJARDINS, ARTHUR U. The action of roentgen rays on inflammatory conditions. *Radiology*, March, 1942, *38*, 274–280.

The use of roentgen rays for the treatment of acute inflammations was first practiced in Europe and roentgen treatment for both acute and chronic inflammations was not generally adopted in this country until after the first World War. But there is no longer any doubt that roentgen treatment is of value in many kinds of acute and chronic inflammation.

The author discusses the mechanism of this action on the basis of experimental and clinical work done at the Mayo Clinic. He published an article on the subject in 1931 but further work has led to a revision of some of the conclusions reached at that time. He now believes that the chief action of the rays in both acute and chronic inflammation is on the leukocytes. These cells are extremely sensitive to the action of roentgen rays, the lymphocytes being somewhat more sensitive than the polymorphonuclear leukocytes. As long ago as 1905 Warthin showed that there are signs of degeneration of leukocytes within fifteen minutes of irradiation; the damage must have begun therefore at once and there is no such thing as a latent period. The greater the degree of leukocytic infiltration, the greater the effect of irradiation. That is why acute inflammations are more amenable to roentgen treatment than chronic ones. In chronic inflammations there are varying degrees of leukocytic infiltration, proliferation of connective tissue and hyaline, caseous or calcareous degeneration. The products of cell degeneration are not affected by irradiation and connective tissue cells are much less sensitive than leukocytes. Connective tissue proliferation tends to decrease the action of irradiation.

The author believes that the action in acute and chronic inflammations must be fundamentally the same. The cells of the vessel walls are much less sensitive to irradiation than the leukocytes and there has been no convincing evidence presented that the former are affected by irradiation.—*Audrey G. Morgan.*

PENDERGRASS, EUGENE P., and HODES, PHILIP J. Acute postoperative parotitis. *Radiology*, March, 1942, *38*, 307–313.

The authors have given roentgen treatment to 47 patients with acute postoperative parotitis. Among these 19 (40 per cent) responded quickly within four days and in 13 (28 per cent) the course of the disease was somewhat shortened. Therefore 32 (68 per cent) were benefited by the treatment. Fifteen (32 per cent) showed little effect and in 7 cases it was necessary to incise and drain the gland. Death from parotitis is rare; more frequently it is due to the primary disease.

To get the best results from roentgen treatment careful oral hygiene must be observed and Stensen's duct must be opened and kept patent. This was not done in all the above cases. Results have been better in recent cases in which good parotid drainage has been maintained. After drainage is established treatment is given with 130 kv., filtered through 0.25 mm. copper and 1 mm. aluminum. The target-skin distance is usually 25 to 30 cm. and the field extends well beyond the inflamed area. A dose of 150 r in air without backscatter is given the first and second days and about 100 r the third day, no treatment on the fourth and sometimes on the fifth day 75 to 100 r.—*Audrey G. Morgan.*

KELLY, JAMES F., and DOWELL, D. ARNOLD. The x-ray treatment of acute peritonitis. *Radiology*, March, 1942, *38*, 299–306.

The authors report 290 cases of peritonitis treated with roentgen rays from 1934 to 1940. The value of roentgen treatment in gas gangrene has been demonstrated conclusively and they call attention to the fact that both acute peritonitis and gas gangrene are mixed infections in which anaerobes play an important part. Roentgen irradiation seems to have a good effect on any infection caused by these organisms. In this report they consider only cases of peritonitis following appendicitis.

The best stage for the use of roentgen treatment is that of early acute spreading peritonitis in the serosanguineous state. Without roentgen treatment in this stage the mortality is 40 to 50 per cent; with roentgen treatment it has been reduced to 10 per cent or less.

The plan of treatment varies in different cases. The number of treatments per day varies from one to three, the dosage from 50 to 75 r, occasionally less, sometimes more; kilovoltage 90 to 130; filter 2 to 5 mm. aluminum; distance 40 to 50 cm.

In the group discussed the mortality when surgery was used, supported by general measures but without roentgen irradiation or sulfonamides, was 68.1 per cent, when sulfonamides, surgery and general measures were used

38 per cent, when roentgen irradiation, surgery, sulfonamides and general measures were used 33.3 per cent and when roentgen irradiation, surgery and general measures were used without sulfonamides 20 per cent. Obviously when roentgen irradiation is used and sulfonamides omitted the results are better than when both methods are used and roentgen irradiation is much more effective than sulfonamides alone. When both methods are used the sulfonamides should be stopped twelve to twenty-four hours before irradiation is begun.—*Audrey G. Morgan.*

Fricke, Robert E., and Madding, Gordon F. Further observations on the radium treatment of postoperative parotitis. *Radiology*, March, 1942, *38*, 294–298.

Acute postoperative parotitis is a serious condition but not so hopeless as has generally been believed. Its seriousness increases with the severity of the operation which precedes it. A mortality rate of 58 per cent for this country has been widely quoted.

The authors discuss 190 cases treated at the Mayo Clinic from January 1, 1927, to December 31, 1940. Radium was used in 111 of these cases, or approximately 60 per cent and other treatments in 79, or approximately 40 per cent.

Up until recently 50 mg. radium element was used filtered with 1.5 mm. monel metal and 2 mm. lead at a distance of 1 inch from the skin. Four fields directly over the swollen gland were irradiated, the tubes being supported on balsa wood blocks arranged in a square. Treatment was continued for eight hours and 896 r applied to the gland. A second treatment of the same kind was given around the gland. Now the lead filter is omitted and the treatment time decreased to six hours. This gives 972 r over the parotid and the same amount is given to the surrounding tissues.

Among these cases there were 19 deaths, or 10 per cent. Of the patients treated with radium approximately 11 per cent died and of those treated otherwise approximately 7 per cent. These figures are not significant with regard to the value of radium, however, as often radium was given as a last resort in cases in which other treatment had failed. It is probable that only one of these deaths was caused by the parotitis, the others being due to the primary condition for which the operation was performed. Nine of the operations were for cancer. Operations on the colon were the most frequent operation in the fatal cases. The chief cause of death was peritonitis, followed by bronchopneumonia, uremia and pulmonary embolism. In 5 of the cases the parotitis had either cleared up entirely or was progressing satisfactorily at the time of death.—*Audrey G. Morgan.*

Popp, Walter C., and Williams, Henry L. Roentgen therapy for acute sinusitis. *Radiology*, March, 1942, *38*, 290–293.

The reports in regard to the value of roentgen treatment have been quite contradictory. The literature is reviewed and the authors, a roentgenologist and an otolaryngologist working in collaboration, report the results of their own work. In 1940 they reported the results in 56 cases and they now report the 43 cases treated since that time. Both groups are divided into moderately severe and very severe cases and details are given in regard to the results. The results were good in 35 of the first series of cases, or 62.5 per cent, and in 35 of the second series, or 81.4 per cent. The conditions of treatment were the same in the two groups, 50 r in cases in which there had been symptoms for one to five days and 75 to 100 r in cases in which the symptoms had persisted for more than five days. One to three treatments were given on alternate days with voltages of 130 kv. (constant potential) filtered through 6 mm. aluminum for adults and 4 mm. aluminum for children, distance 40 cm. The only difference was in the fields. In the first series treatments were given through one field to cover both frontal areas and one field each for the maxillary sinuses, the eyes and eyebrows being carefully protected. In the last series two fields were used, covering the whole face divided vertically into two equal parts. Treatments were given at an angle of about 45°, converging toward the nose. The eyes were not protected. This method gives a better irradiation of all the sinuses and the natural ostia and to it the authors attribute their greater success in the second series.—*Audrey G. Morgan.*

Rousseau, J. P., Johnson, W. M., and Harrell, George T. The value of roentgen therapy in pneumonia which fails to respond to the sulfonamides. *Radiology*, March, 1942, *38*, 281–289.

Two groups of cases are discussed, one in which no treatment was given except roentgen irradiation and one in which the irradiation

was given after the patients had failed to respond to sulfonamides.

The first group of 104 patients showed 98 recoveries and 6 deaths, a mortality of 5.7 per cent. This was much lower than the previous ten year mortality rate of 28 per cent for pneumonia in the same locality. Improvement was often noticed by the patient before there was any change in temperature, pulse rate or physical findings. Leukopenia and bacteriemia were unfavorable prognostic signs. The roentgen treatment had no bad effects in any of the cases.

In the second group of 29 cases which had failed to respond to sulfonamide treatment in three to seven days there were 22 recoveries and 7 deaths, or a mortality rate of 27.1 per cent. All the patients who died did so within less than fifteen hours after irradiation which suggests that they may have been hopeless before irradiation was given. While the sulfonamides are of great value in the treatment of pneumonia these cases indicate that roentgen treatment should be used for patients who do not tolerate sulfonamides well, and in old people and patients with serious disease of the heart, liver or kidneys. There is apparently no contraindication to the use of roentgen treatment in patients who have been given sulfonamides previously but until more is known about the reactions to these two forms of treatment the drug should be stopped before irradiation is given.—*Audrey G. Morgan.*

QUIMBY, EDITH H. Some practical considerations regarding the employment of various qualities of roentgen rays in therapy. *Radiology*, March, 1942, *38*, 261–273.

The problem in radiation treatment is to give an adequate dosage to the lesion without injuring normal structures. Unfortunately it has been the custom in stating dosage to give only the amount of radiation delivered in air or to the skin, without taking into consideration the amount that actually reaches the tumor. With the same amount of radiation delivered to the skin the amount that reaches the tumor may vary greatly, depending on the voltage used, the filtration, the distance of the lesion from the surface, and other factors. For instance two patients might be given 1,000 r measured in air with the supposition that they were being given the same dose. But if in the first case the lesion was 2 cm. below the surface in a field of 25 sq. cm., and the other 7 cm. below the surface in a field of 100 sq. cm. the first lesion would be given from 50 to 150 per cent more than the second, depending on the quality of the radiation and the focal-skin distance.

Tables showing the tumor dose at varying depths for radiation ranging from 100 kv. unfiltered to 200 kv. highly filtered have been worked out. Charts are given for six voltage-filter-distance combinations, their application to different forms of tumor indicated and directions given for working out from them different sets of factors. Figures are given both for depth dose in percentage of skin dose, that is the number of roentgens delivered at any depth per 100 r on the skin, and for depth dose in percentage of air dose, that is the number of roentgens delivered at any depth for each 100 r in air.

In the discussion Dr. Ernst emphasized the value of such depth dose curves, the importance of accurate tumor dosage and the necessity for the radiologist working with the physicist when a calibration of his apparatus is made.—*Audrey G. Morgan.*

GUTHMANN, HEINRICH, and SCHMIDT, WILHELM. Das Verhalten des weissen Blutbildes bei der therapeutischen Kurzwellenbehandlung. (The white blood picture in therapeutic short wave treatment.) *Strahlentherapie*, 1941, *69*, 381–392.

Short wave treatment has proved effective in inflammations of the genital tract. It is particularly valuable in subacute cases; some caution is necessary in dosage in acute cases.

The author studied the fluctuations in the white blood picture during the treatment as an index of the state of the inflammation and the reactive capacity of the body. The cases are divided into groups depending on the original blood count and the clinical signs of inflammation. Blood counts were made just before and just after treatment and two and four hours later. Tables are given showing the details of the results.

There was always a decrease in the number of leukocytes on treatment followed by a rise. The cases with high values to begin with showed a greater fall and a final readjustment at a lower level, while the cases with low values in the beginning fell less and the secondary rise, after two hours or more, was greater.

The decrease in the peripheral blood count in all the groups was probably due largely to withdrawal of leukocytes from the peripheral to the splanchnic area. Other factors are probably the dilatation of the capillaries that takes place on treatment, the shifting of ion concentrations and chemotaxis on the part of the inflamed focus. The hyperemia caused at the site of inflammation by the dilatation of the capillaries is a desirable result, and it certainly has a marked effect on the migration of the leukocytes and their distribution. A transition from a chronic to an acute stage of the inflammation is indicated by the marked increase in leukocytes in the cases with moderate and low values. This is also indicated by the slight shifting to the left and the decrease of eosinophile cells. Probably the great increase of cells in the cases with low values is to be attributed to a considerable degree to stimulation of the bone marrow and consequent increased output of cells.—*Audrey G. Morgan.*

Gauss, C. J. Vierzig Jahre Strahlenbehandlung des Genitalkarzinoms. (Forty years of radiotherapy of genital carcinoma.) *Strahlentherapie*, 1941, *69*, 365–380.

The author, Director of the Gynecological Clinic at the University of Würzburg, pays tribute to the courage of Döderlein in giving up surgery of genital carcinoma for radiotherapy at a time when he was one of the leading surgeons in that field and when radiotherapy was still, and with some justice, unpopular. He reviews the history of the development of radiotherapy from its crude beginnings when apparatus was quite inadequate and the abdomen was opened in the operating room and the patient wheeled to the roentgen room and irradiation applied directly to the uterus. In some cases eosin solution was injected into the uterine cavity as it was thought to make the mucous membrane more sensitive to irradiation. From that to modern protracted fractional technique is a long journey and much still remains to be accomplished. But statistical tables are given from his own clinic at Würzburg, and from those of Döderlein at Munich, Eymer at Heidelberg, Wintz at Erlangen and some collections of statistics from various clinics which show that the results from radiotherapy alone or in association with surgery are better than those of surgery alone. In some groups the number of relative cures by surgery, that is the proportion of cures to cases treated, is equal to or even somewhat higher than that by radiotherapy, but when the absolute figures are considered, that is the proportion of cures to total number of cases seen, the superiority of radiotherapy is shown. One of its great advantages is that a considerable percentage of inoperable cases, which were hopeless under surgical treatment, can be cured. Statistics are given for carcinoma of the cervix and body of the uterus, carcinoma of the ovary and epithelioma. They show that radiotherapy has become the treatment of choice in chorionepithelioma.—*Audrey G. Morgan.*

Rajewsky, B. Physikalische Diagnostik der Radiumvergiftungen. (Physical diagnosis of radium injuries.) *Strahlentherapie*, 1941, *69*, 438–502.

In 1935 the author was commissioned to establish a research laboratory for the physical diagnosis of radium intoxications at the Institute for Biophysics at Frankfurt a. M. He describes in detail the methods and apparatus in use there, giving photographs and diagrams of the apparatus used, including the radium stethoscope. By the use of these methods it is possible to determine the radium excreted from the body in the urine and feces as well as the radium content of the blood, the radium emanation in the blood, expired air, urine, sweat, feces and the direct excretion of emanation through the skin and to measure the gamma radiation given off by the body. Workers in radium institutes can be tested for the purpose of preventing injury and patients who have already been injured can be examined for the extent of the injury. Postmortem examinations can also be made. Deposits of as much as 1μg radium-equivalent are harmful, so it must be possible to measure down to as little as 0.1μg radium-equivalent. The examination for radium diagnosis is preceded by a medical examination. Radium rooms are also measured for the radium content of the air and the directors warned that it must be kept below a certain amount by ventilation. The working personnel are also instructed to avoid as far as possible the swallowing of dust charged with radium and contact of the skin, especially if broken or fissured, with radium-containing substances.—*Audrey G. Morgan.*

BORAK, J. Radiation effects on blood vessels. Part 1. Erythema; edema. *Radiology*, April, 1942, *38*, 481–492.

The various theories advanced to account for the effects of radiation on the blood vessels are discussed. There are three waves of erythema. The first, which often occurs within a few hours after irradiation, is due to dilatation of the capillaries. It is independent of the quality of the rays and also, largely, of the dose. It is not affected by mechanical compression of the arteries nor by constricting them with adrenalin or cold. The second erythema which does not occur until after a week or two results from constriction of the arteries. The second erythema can be suppressed, or at least delayed or weakened by compression, cold or adrenalin. It requires about 25 per cent more radiation energy to produce it with hard rays than with soft. The third erythema results from the action of the rays on the veins. It does not appear until four weeks, or even more, after irradiation.

There is also edema after irradiation which is more marked the greater the radiosensitiveness of the cells irradiated. This suggests that at least one important factor in causing post-irradiation edema is increased osmotic pressure outside the vessels due to the decomposition of intracellular proteins. Edema may occur without erythema but erythema is always accompanied by edema.

If the permeability of the capillaries is greatly increased there is great loss of fluid, resulting in increased concentration of the blood. This increased concentration of the blood is the first of a series of processes which causes irradiation sickness.—*Audrey G. Morgan.*

KAUTZKY, A. Hautreaktion und Wellenlänge bei fraktionierter Röntgenbestrahlung. (Skin reaction and wave length in fractionated roentgen irradiation.) *Strahlentherapie*, 1941, *69*, 423–430.

Experiments are described in which small skin fields were irradiated with waves of varying hardness up to the threshold of epidermolysis. The fields irradiated with the harder rays showed a more intense reaction but the maximum of the reaction appeared later.

The more intense reaction was due to the greater depth dose with the harder radiation. The tissue reaction is dependent on the volume of tissue irradiated. This difference is probably not due to a difference in the biological reaction of the two kinds of radiation. The difference in the time of the reaction seems to be the essential biological difference between soft and hard radiation. The time of appearance of the maximum reaction is apparently delayed with decreasing wave length, that is for increasing degrees of hardness of radiation.—*Audrey G. Morgan.*

MAYER, ERNST G. Über quantitative und qualitative Reaktionsunterschiede nach Röntgenbestrahlung. (Quantitative and qualitative differences in reaction after roentgen irradiation.) *Strahlentherapie*, 1941, *69*, 431–437.

The author discusses marked differences in reaction to roentgen rays on the part of different patients, particularly in Coutard's irradiation of carcinomas of the upper respiratory tract and esophagus. He cites 2 patients with carcinoma of the vocal cords. The first reacted to 7,200 r_0 given in twenty-eight days with only moderate hyperemia, while the second reacted to 3,900 r_0 with extensive membrane formation. The later course was so violent that the irradiation had to be given up on the twenty-second day though he had been given less than 6,000 r_0. Some roentgenologists have held that irradiation by Coutard's method is not effective unless membrane formation is produced but the author feels sure it would be dangerous to continue irradiation to that extent in some cases.

As a rule, the reaction of the mucous membrane runs parallel with that of the outer skin but there are some patients who show an intense mucous membrane reaction with only a slight skin reaction, and vice versa. There are also great variations in the time at which the reaction begins. If infection supervenes on an area that has been irradiated with quite large but not excessive dosage there may be an intense reaction. A case is described in which such a reaction ended in death.

In cases of tumors of the larynx or other parts of the body, there may be a swelling around the tumor. Sometimes this recedes under roentgen treatment but in some cases it increases progressively. In such cases the prognosis is bad and the dosage should be decreased or the treatment stopped.

Such atypical reactions help to explain failure of the desired effect to take place in some cases. —*Audrey G. Morgan.*

Meyer, Wm. H. Roentgen dose fractionation for varying periodicities. *Radiology*, Feb., 1942, *38*, 191–200.

For the past ten or fifteen years the fractionation method of roentgen treatment has replaced the older methods. There are great variations in the sensitiveness of different cells, tissues and organs to irradiation. The best measure of the biological reaction to irradiation is the reaction of the human skin. The number of roentgens measured by physical methods required to produce a given skin reaction varies greatly, depending on various factors, not only variations in voltage and filter but also the size of the area irradiated and the intensity of the dose or the time factor (r/m).

In this article charts are given showing the period of time required for the production of a given skin reaction under different conditions of fractionation. They are based on 366 clinical cases and the author believes they are correct to within a ± 10 per cent variation. The r dose required to produce a skin unit dose varies from less than 300 r for 50 kv. to 1,000 r at a million volts and with strong filtration.

With larger doses the reaction is sharper and more of the peak type while with smaller fractions, below one-half the skin unit dose, one or two more treatments could be given without exceeding the limit of skin tolerance. It is doubtful whether any one method of fractionation is superior to others except that with smaller fractions repeated frequently a longer time is required which makes better control possible by observing the reaction. The charts here given show time variations of from one to six weeks—*Audrey G. Morgan.*

Ernst, Edwin C. The roentgen management of uterine fibroids. *South. M. J.*, Dec., 1941, *34*, 1249–1255.

The author discusses the treatment of 500 cases of fibromyoma of the uterus treated from 1928 to 1935. Roentgen irradiation has proved very successful in these cases. In approximately 97 per cent of them the results varied from 50 per cent reduction in the size of the tumor to its complete disappearance. The great majority of the patients are clinically cured. Many of these patients have been under observation for fifteen years or more. Operation was necessary in 3 cases. When there is any doubt as to malignancy or any ovarian complications, operation should be performed. Irradiation should not be used if there is calcification in the tumor nor should it be used for subserous or submucous myomata, especially if they are pedunculated.

Two positive cases of malignancy and one doubtful one developed in this series of 500 cases after irradiation, but there were approximately only one-tenth as many complications with cancer as in non-irradiated cases. Roentgen therapy is not contraindicated in mild pelvic infection.

The author believes that the fractional treatment of uterine fibroids is to be preferred to treatment with a single large dose of either roentgen or radium radiation. He usually gives two to four series of 125 r each at intervals of three weeks. The series of 125 r is given in four to six treatments. The physical factors used are 165 kv., 0.75 mm. copper filter, half-value layer 0.5 mm. copper, through anterior and posterior fields. Two posterior and one anterior field may be necessary for large patients. Occasionally a combination of roentgen and radium therapy is indicated. The smaller and more fractionated the dose the less trouble is to be expected from postmenopausal disturbances.—*Audrey G. Morgan.*

Brown, Willis E., Kretzschmar, N. R., Peck, Willis S., and McGreer, John T. Irradiation of benign pelvic lesions. *Am. J. Obst. & Gynec.*, Feb., 1941, *41*, 295–300.

The authors reviewed the records of 334 patients treated with roentgen rays or radium for benign pelvic lesions. Their objective was: (1) to determine the efficiency of irradiation in the control of uterine bleeding; (2) to evaluate the menopausal symptoms which might ensue, and (3) to improve their method of applying roentgen radiation for the purpose of castration.

As for the first objective, i.e., the efficiency of irradiation in controlling uterine bleeding, it was concluded that at least 625 to 749 r to the ovary is necessary to assure permanent castration. This is larger than the doses reported in the literature as being necessary to produce this result. Regarding radium dosage, it was felt that 1,500 to 2,000 mg-hr. should be sufficient for castration in most instances.

In the second objective, an attempt was made to evaluate the clinical symptoms following castration in this series of patients since the opinion is fairly widespread that the psychic changes observed after irradiation are much

more pronounced than after surgical castration or after the normal menopause. Seventy-three per cent of the patients castrated as a result of irradiation developed hot flushes while 62 per cent of the patients who had been irradiated but were not castrated as a result developed this symptom. In the study of surgical castration, 86 per cent of the patients developed hot flushes after bilateral oöphorectomy and 58 per cent developed them after hysterectomy with ovarian conservation. Thus it would seem that the incidence of hot flushes after castration by irradiation is somewhat less than that following bilateral oöphorectomy. Concerning libido, the surgical and irradiation effects were found to be about the same; 42 per cent of the castrated females in the irradiated series reported a decrease in libido and 36 per cent of the noncastrated reported a decrease in this function.

Objective number 3: A new technique was employed to overcome the temporary bladder, bowel and skin irritation which occurred in some of the patients who received 600 to 1,000 r to each of two pelvic fields delivered within a few days. This consisted of dividing the lower abdomen into six fields instead of two (two anterior, two posterior and two lateral). In this way, the necessary anterior and posterior skin dose was reduced by one-third.

In their discussion, the authors state that (1) irradiation is an efficient means of curtailing benign uterine bleeding; (2) irradiation is most applicable to a woman of forty or over, at which age she is to be considered as approaching the menopause; (3) irradiation is to be preferred to surgery in the menopausal patient because it is efficient, it is without risk, and it is cheaper; (4) a diagnostic dilatation and curettage should precede irradiation; (5) surgery is preferable in palpable disease of the adnexa; (6) surgery is to be preferred when a fibromyoma exceeds the size of a two and one-half months' pregnancy; (7) in a young female, even small doses of radiation are to be eschewed—*Mary Frances Vastine.*

VONESSEN, A. Über die Bedeutung von zentralen Krebsuntersuchungsstellen für eine wirksame Krebsbekämpfung. (The importance of central clinics for examination for cancer in successfully combating cancer.) *Strahlentherapie*, 1941, *69*, 528–540.

The author emphasizes the value of establishing clinics for examination for cancer in connection with large city hospitals and making known to the public that such clinics for free examination exist. One death out of nine is from cancer and its diagnosis is therefore a public health question of the greatest importance. Statistics are given showing how rapidly the prospects for cure decrease as the disease advances and how large a percentage of patients do not come for treatment until the most hopeful stage has passed.

Experience with such free cancer clinics which have been established in connection with the hospitals in the city of Hamburg has shown that when such clinics are established and advertised a greater percentage of the patients come for treatment in the early and hopeful stage. A simple announcement in the newspapers by the public health authorities that such clinics had been established resulted in a large number of patients coming to them. It is true that at the St. George Hospital, of the 375 patients who came for consultation during the first fifty clinic hours only 10 per cent had cancer, but most of these were in the first stage and otherwise would probably not have been examined until a later stage. Moreover some pathological condition that required treatment was found in almost all the cases.

These clinics should be established in connection with large hospitals so that the patients may have the advantage of consultation with and treatment by experts and so that the necessary facilities may be available for all sorts of examinations. There should also be close collaboration between these clinics and the public health authorities.—*Audrey G. Morgan.*

SCHINZ, H. R. Krebsvorschau. (Prospects for cancer.) *Strahlentherapie*, 1941, *69*, 521–527.

The absolute number of cancer cases in Zürich was 150 in 1895 and 370 in 1931. This city has about 320,000 inhabitants and in 1938 about 500 of them died of cancer. In the whole of Switzerland with its 4,200,000 inhabitants 6,800 died of cancer in that year. That is, for every 10,000 inhabitants the number of cancer deaths in 1938 was 16. In Zürich about one person dies every day of cancer and in the whole of Switzerland about 19 per day. In Zürich every sixth or seventh death is from cancer. In Swiss statistics only carcinoma is counted as cancer while in other countries sarcoma, glioma and other malignant tumors are included.

A part of this increase is due to the changing

character of the population. Infant mortality and the mortality from tuberculosis have been greatly decreased. As a result of this, of the decreasing birth rate and the increased length of life brought about by medical care, there are many more old people in the population in proportion to the young than there were formerly. This tendency will continue and it is estimated by statisticians that the population of Switzerland will have reached its maximum in 1940 and will then slowly decline. Statistical tables are given by ten year age groups for the population in Switzerland from 1900 up to 1960 and for the deaths from cancer over the same period. It is estimated that the 4,085 deaths from cancer in 1900 will have grown to 8,855 by 1960. Instead of the 19 persons that die daily in Switzerland from cancer 24 will die per day in 1960. The practical conclusion from this with regard to hospital construction is that the number of beds will have to be increased by 29 per cent for 1960 as compared with 1940 and instead of the 40 beds that he has in his radiological clinic in Zürich the author will need about 52. All this of course is on the assumption that no more effective treatment is found for cancer before 1960. The possibility of finding such a treatment always exists.—*Audrey G. Morgan.*

Uhlmann, Erich. Significance and management of radiation injuries. *Radiology*, April, 1942, *38*, 445–452.

In spite of improvement in apparatus and technique there are still many injuries from roentgen and radium burns. The author has seen 70 such cases in the Tumor Clinic of the Michael Reese Hospital in Chicago in the past three years. Half of them were in physicians, only 3 in roentgenologists. This is probably because many physicians are not familiar with the technique of treatment and protective measures.

There is little tendency to spontaneous healing in these injuries, probably because of destruction of the capillaries and consequent poor circulation.

Until recently there has been no effective treatment for such injuries. Since 1928 the author has been using radon absorbed in vaseline in treatment. More than 90 per cent of the emanation from radon is alpha rays which are corpuscular and not of the wave form of roentgen and radium rays. The concentration is about 100 electrostatic units per gram of vaseline, equal to 0.0364 mcd. It would take about 25 such doses to cause erythema of the skin. From two to ten or more weekly applications are given. Between treatments boric acid ointment is used. No harm has resulted to any patient and all have responded well to the treatment. Equally good results have been obtained in a United States Army Hospital where the treatment has been used.—*Audrey G. Morgan.*

Cocchi, Umberto. Woran stirbt der Krebskranke? (What causes the death of the cancer patient?) *Strahlentherapie*, 1941, *69*, 503–520.

A study was made of the case histories and pathological findings in 373 cases of malignant tumor to determine the cause of death. In one-third of the patients the immediate cause of death was some pulmonary complication, in one-fourth cachexia, with or without generalized metastasis, while one-tenth died from hemorrhage, about 6 per cent from heart complications and 3 per cent from pulmonary embolism. In young persons the most frequent immediate cause of death was cachexia, while among the older patients the majority died of lung complications. The chief cause of death in malignant tumors of the upper respiratory tract, the esophagus and the bronchi is pulmonary complications, while in tumors of the breast the most common cause is cachexia. In tumors of the esophagus hemorrhage is a frequent cause of death.

Three-fourths of all the patients died of cancer, either directly as a result of generalized metastasis, asphyxia or carcinomatous peritonitis (about 23 per cent) or indirectly as a result of pulmonary, cardiac or other complications, such as hemorrhage. In the other fourth the patients died of intercurrent disease or other complications not caused by the cancer. This included one-seventh of the pneumonia cases and 40 per cent of the cases of heart failure.—*Audrey G. Morgan.*

Auler, H., Schilling, W., and Woite, Ch. Über die Behandlung von Strahlengeschwüren, Verbrennungen und anderen schlecht heilenden Wunden. (The treatment of ulcers from irradiation, burns and other wounds that heal poorly.) *Strahlentherapie*, 1941, *69*, 417–422.

Wounds heal naturally from the action of the

blood, lymph and surrounding cells if there are no disturbing factors present. In treating them physiological conditions should be restored as nearly as possible. The most effective of all healing substances therefore is blood plasma. In radiation necrosis healing is interfered with by injured cells and generally by secondary infection. Of course the wound or ulcer must be cleansed before treatment. It should also be tested as to sensitiveness to fat or oil and if it is sensitive, salves containing these substances should not be used. If a gelatinous substance is being excreted, the wound should be cleansed before treatment by scattering sugar over it.

The authors' plan of treatment is as follows: The wound is first irrigated with rivanol-salt solution and covered for several hours with a salt solution compress. Then blood plasma is dropped on it with a pipette and it is left open until coagulation takes place. The tissue around the wound may be covered with lebertran salve, or if it is sensitive to fat, with eucerin-calcium salve. A salt solution compress is laid on the plasma-covered wound. On changing dressings the next day, the wound is cleansed with salt solution and covered for half an hour to an hour with a salt solution compress. If it is then clean, plasma may be dropped on it again. Otherwise it is treated with 3 per cent pellidol salve or some other stimulant salve and the plasma treatment continued after twelve to twenty-four hours.

Severe large radium necroses have been treated successfully by this method and second and third degree burns have been healed without contractures. Five illustrative cases are described.—*Audrey G. Morgan.*

PICKHAN, ARTHUR. Die Strahlenbehandlung der primären Krebse der weiblichen Harnröhre. (Radiotherapy of primary cancer of the female urethra.) *Strahlentherapie*, 1941, *69*, 393–399.

Primary cancer of the female urethra is quite rare. It generally originates from the pavement epithelium of the external opening of the urethra. The symptoms are slight at first and about a third of the patients do not come for treatment until the inguinal glands are involved. Surgical treatment of this form of cancer has been most unsatisfactory.

For the past five years the author has been treating his cases with radium. Six cases treated in this way are described and another referred to. The amount of radium used varies with the size of the tumor. It is filtered through 1.5 mm. brass. It is applied either at a distance or through a mushroom shaped mould fitted to the anatomical part so that irradiation is given both inside and outside the urethra. In some cases needles are used. The dose varies, depending on the case, from 600 to 2,000 mg-hr. Sitz baths, salves or powder are used in the after-treatment.

Three of the cases are free of recurrence after an average period of more than forty-seven months. One patient has been free of recurrence for fifteen months and another for seventeen months. One has been treated only recently. There was death soon after treatment in 1 case, which was probably no longer suitable for treatment.

These results are better than those from any previous method of treatment.—*Audrey G. Morgan.*

BEUTEL, ALOIS. Der Blutcholesterinspiegel als Indikator der strahlentherapeutischen Beeinflussung der Hyperthyreosen. (The blood cholesterin content as an indicator of the effect of radiotherapy in hyperthyroidism.) *Strahlentherapie*, 1941, *69*, 400–406.

It was found some time ago that the cholesterin content of the blood is increased in hypothyroidism, particularly pronounced myxedema. More recent examinations have shown that in the majority of cases of Basedow's disease and other forms of hyperthyroidism the cholesterin content of the blood is decreased, in a much smaller number of cases increased; it is very rarely normal. The severity of the clinical symptoms runs parallel with the decrease in the blood cholesterin content.

The author made a study of a series of cases to determine the effect of radiotherapy on this abnormal cholesterin content of the blood. Tables are given showing the details of the results. He found that even small doses of 40 to 60 r given three to four times affected the blood cholesterol content. The cases with low cholesterin content showed a relatively rapid rise to hypernormal values, which then gradually fell to normal. The cases with a high cholesterin content reacted much more sluggishly. The method of determining the blood cholesterin content, which is a modification of Bloor's method, is described.—*Audrey G. Morgan.*

MISCELLANEOUS

Mutscheller, A. Recovery function of irradiated tissues: a theoretical and experimental study. *Radiology*, Jan., 1942, *38*, 53–73.

This is a technical discussion of the recovery function of irradiated tissues illustrated with graphs, tables and mathematical formulae designed to show the relation between amounts of radiation measured physically and the biological effects of such radiation. An attempt is also made to give a clear idea of what is meant physically, chemically and biologically by injury and recovery of cells.

The curves for cell killing differ for different tissues. The shape of the curves is dependent on variations in the mass-roentgens which reach the cells and on the rate of cell recovery. Absorption curves in water are given and the number of roentgens stopped in each centimeter of water are called mass-roentgens. The term is also applied to the number of roentgens absorbed in 1 cm. of tissue at various depths.

If the rate of mass-roentgens falls below a certain figure there may be no tissue reaction. The effectiveness of the radiation increases with increase in mass-roentgens and decrease in recovery rate. If the intensity of radiation and the absorption factor are so adjusted that the ratio of mass-roentgens to the recovery coefficient of each tissue is equal, the same biological effects will be produced. But various fractions of radiation which give the same total do not produce the same biological or qualitative changes.

The recovery factor γ is a statistical factor that indicates the rate of recovery of skin or other tissues when they are injured but not killed by radiation. The recovery factor seems to be merely a measure of the sum total of the functions which control the recovery of the cell from injury by radiation. Its relationship to the other properties of cells, such as growth, karyokinetic action and function, cannot be defined. The value of the recovery factor for healthy adult human skin is determined by the quantities of radiation required for equal biological results in various irradiation times.—*Audrey G. Morgan.*

Stenstrom, Wilhelm, King, Joseph T., and Henschel, Austin F. The correlation between roentgen dosage and lymphoid cell migration in tissue cultures. *Radiology*, April, 1942, *38*, 477–480.

Mesenteric lymph nodes of adult rabbits were used as experimental material for determining the effects of various dosages of roentgen rays on migration of the lymphoid cells *in vitro*. Matched fragments were taken from the nodes and one set used for experimental purposes and the other for controls. This is important as the structure and therefore the effects of irradiation are different for cortex and medulla. The fragments were put in flasks of serum and irradiated, the controls being protected by lead plates. Cultures were then made in heparinized plasma to which three drops of serum-chick embryo extract had been added. The experiments were carried out over three or four years. Tables are given showing the length of exposure and number of roentgens given and the amount of inhibition of migration in the experimental fragments as compared with the controls. The irradiation not only decreases the width of the migration zone but the rims become progressively thinner as the dosage is increased. The average spread of inhibition for all dose levels was 6 per cent. A dose of 39 r caused an inhibition of 8.8 per cent. Inhibition increases rapidly with increased dosage up to about 620 r and much more slowly after that.

Apparently there are two groups of celis in mammalian lymph nodes which differ widely in their sensitiveness to the action of roentgen rays. Sensitive cells are inhibited up to doses of about 620 r, while much larger doses are required to inhibit the more resistant ones. The more resistant cells migrate more slowly and their response, if any, to small doses, is masked by that of the more rapidly migrating sensitive cells. It will require histological examination of stained serial sections of cultures at all dose levels to confirm these conclusions. The results of such studies will be published later.—*Audrey G. Morgan.*

Williams, M. M. D. An electric model of an x-ray machine. *Radiology*, March, 1942, *38*, 338–349.

Students often learn more from doing things in a laboratory than from reading and lectures. Students of radiology should study the construction of different kinds of roentgen-ray equipment and determine the effect of various types of rectification on the quantity and qual-

ity of the roentgen rays produced. To help students in this work the author has built a model from radio parts which functions electrically much like a roentgen machine except that the voltages are low and can be changed easily to demonstrate many of the rectifying circuits commonly used. The use of an oscillograph with the model shows the wave forms of the voltage and current in any part of the secondary circuit.

The model is described in detail and illustrated and diagrams of the wiring shown. A list of the equipment is given. Except for the main transformer, the autotransformer and the control box for the oscillograph all the equipment is standard and can be bought at any radio store. The total cost of all the equipment except the oscillograph and the control box for it was less than $90.—*Audrey G. Morgan.*

TAFT, ROBERT B. A portable Geiger-Müller counter. *Radiology*, March, 1942, *38*, 350–352.

A portable instrument for the detection of radium is described and illustrated and a self-explanatory wiring diagram given. The principle involved is the same as that in the more complicated laboratory instrument. This little instrument has proved successful in the recovery of much radium and if kept in good condition and tested every few weeks it is a great potential safeguard to all the radium in the community.

Its sensitivity is the same as that of other counters described by the author. Sensitivity means the ability to double the normal count when 50 mg. radium is located at a distance of about 212 feet, this count being directly proportional to the amount of radium and inversely proportional to the square of the distance.—*Audrey G. Morgan.*

SCHWARZSCHILD, M. M. Tube ratings and exposure. *Radiology*, Jan. 1942, *38*, 84–85.

In roentgenography in general, as well as in the special methods of kymography and fluorography, the results are improved if the full rating of the tube is utilized. The manufacturers usually give this information in the form of graphs that show voltage, current and exposure time. But rating charts would be more directly useful if instead of showing voltage, current and time they showed voltage, charge (milliampere-seconds) and time. Such a type of chart is shown as well as another in which focal spot size is introduced as a new parameter. These use minimum exposure time as a variable and the objection has been made that this use of minimum exposure is misleading, for an inexperienced person may think that the tube can be used for a longer time with the same voltage and current. To overcome this difficulty the chart may be constructed with maximum current instead of minimum time as the other variable. This type of chart is also illustrated. All of these charts give information that is more directly useful than that given in the usual manufacturers charts.—*Audrey G. Morgan.*

WILLIAMS, M. M. D. Two instruments for measuring x-ray tube voltage. *Radiology*, Jan., 1942, *38*, 80–83.

Two instruments are described, one a calibrating device for use with an oscillograph and the other vacuum tube peak voltmeter. The wiring diagram of each of these instruments is given. Both have been in use for the past year and a half at the Mayo Foundation and both have proved satisfactory. Technical details in regard to their use are given.

The vacuum tube peak voltmeter is easily transportable and determines peak voltages accurately and quickly. But it measures only peak volts. Measurements with the oscillographic equipment are in general easier and quicker to make. By means of the oscillograph it is also possible to observe the voltage wave form, which is often of more value than the determination of the peak voltage.—*Audrey G. Morgan.*